A STUDY OF THYROID PROFILE IN PATIENTS WITH ACUTE CORONARY SYNDROME

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BONAFIDE CERTIFICATE

This is to certify that **"A STUDY OF THYROID PROFILE IN PATIENTS WITH ACUTE CORONARY SYNDROME "** is a bonafide work done by **Dr.N.SHEIK SULTHAN ALAVUDEEN**, post graduate student, Department of General Medicine, Kilpauk Medical College,Chennai-10, under my guidance and supervision in partial fulfillment of regulations of **The Tamilnadu Dr.M.G.R.Medical University** for the award of **M.D.Degree Branch I, (General Medicine)** during the academic period from May 2009 to April 2012.

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I, **Dr.N.SHEIK SULTHAN ALAVUDEEN**, solemnly declare that the dissertation titled **Study of thyroid profile in acute coronary syndrome** is prepared by me, This is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine)

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CONTENTS:

Abstract:

Acute Coronary Syndrome is one of the leading causes of morbidity and mortality in India and in worldwide. The thyroid hormonal changes could result in the functional derangement of the cellular metabolism and affecting almost all the organs, the heart in particular. The thyroidal hormonal change occurring in the setting of acute stress condition like sepsis, acute coronary syndrome etc., is termed as Sick Euthyroid Syndrome. This condition is characterized by low T3, raised rT3 and normal levels of T4, FT3, FT4 and TSH. This change in thyroid function is thought to be associated with the mechanism involved in maintaining energy in face of altered systemic homeostasis caused by the acute ischemic event or directly related to inflammatory cytokines, acting as an inflammatory marker or both. This study assessed the prevalence of Sick Euthyroid Syndrome (SES) in patients with Acute Coronary Syndrome (ACS). This study also assessed the distribution of SES in ACS and the correlation between thyroid hormone profiles with the outcome. The prevalence of the Sick Euthyroid Syndrome (SES) is as high as 25% i.e. one quarter of ACS patients had SES. The prevalence of SES in old age group was low as compared to younger population. Sick Euthyroid state significantly associated with High BMI, CRP positivity and this condition associated with worst outcome. Sick Euthyroid state not correlated significantly with sex, diabetic state, hypertension, dyslipidemia and smoking. The T3 and rT3 levels well correlated with the poor outcome among Sick Euthyroid Syndrome patients. Also, the Sick Euthyroid state significantly associated with poor outcome. Hence the Sick Euthyroid State serves as an important predictor of worst prognosis in patients with Acute Coronary Syndrome.

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of mortality and morbidity in the world and acute coronary syndromes (ACS), which encompass unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI), are the commonest causes of mortality in patients with CAD. With the introduction of a huge armamentarium of invasive and noninvasive therapeutic strategies, the mortality related to ACS has significantly reduced in the developed world over the past 20 years. But the mortality remains high among Indians. Acute coronary syndrome (ACS) represents the clinically manifest acute myocardial ischemia.

Several studies have shown the effect of thyroid hormones on morbidity and mortality from heart failure, systemic arterial hypertension, atherosclerosis, dyslipidemia and cardiopulmonary surgeries.

Multiple alterations in serum thyroid function test findings have been recognized in patients with a wide variety of NTI (nonthyroidal illnesses) without evidence of preexisting thyroid or hypothalamic-pituitary disease.

The changes observed in these situations have been classified as “Sick Euthyroid Syndrome”, consisting of low total T3 and/or free T3, increased reverse T3 (rT3), and normal TSH, T4 and free T4 levels. This syndrome has been well described in acute coronary syndrome affecting the prognosis.

This change in thyroid function is thought to be associated with the mechanism involved in maintaining energy in face of altered systemic homeostasis caused by the acute ischemic event or directly related to inflammatory cytokines, acting as an inflammatory marker, or both.

The present work is a modest attempt to study the prevalence of Sick Euthyroid State in patients with acute coronary syndrome.

AIM OF THE STUDY

1. To study the prevalence of Sick Euthyroid Syndrome in patients with Acute Coronary Syndrome.

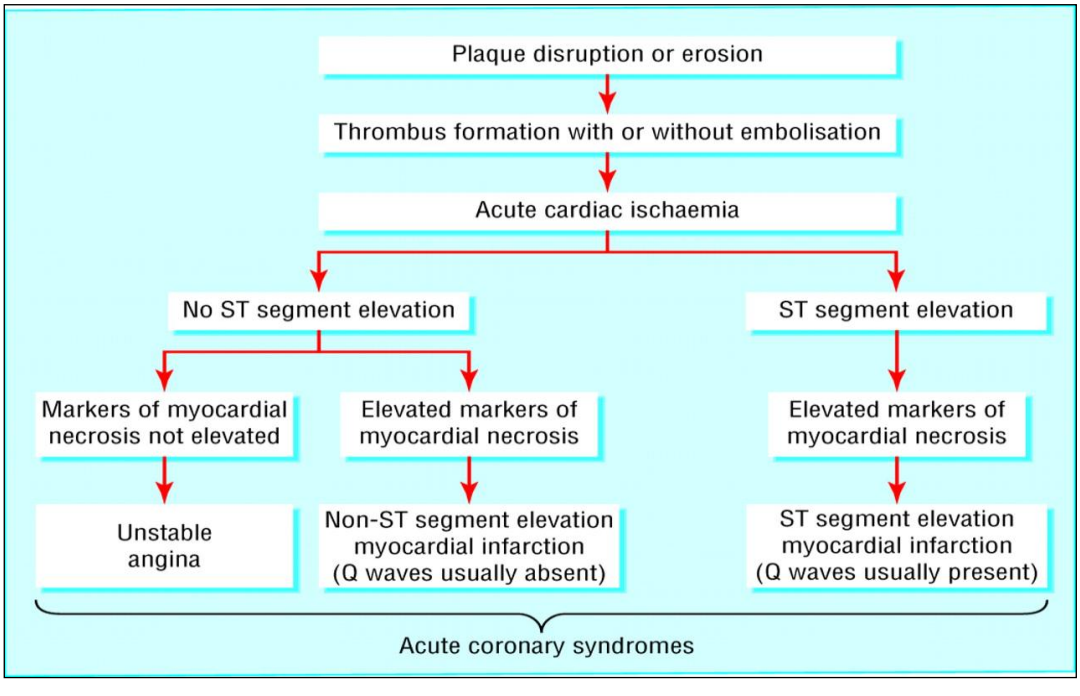
2. To study the distribution of Sick Euthyroid Syndrome according to age, sex, BMI, type of ACS, diabetes, hypertension, dyslipidemia, smoking, CRP status in patients with ACS.

3. To Study the correlation between the thyroid profile and the outcome among the SES patients with Acute Coronary Syndrome.

REVIEW OF LITERATURE

ACUTE CORONARY SYNDROME:

Acute coronary syndrome (ACS)[1] refers to any constellation of clinical symptoms that are compatible with acute myocardial ischemia. ACS is divided into ST- elevated myocardial infarction (STEMI), non-ST elevated myocardial infarction (NSTEMI), and unstable angina (UA).



STEMI results from complete and prolonged occlusion of an epicardial coronary blood vessel and is defined based on ECG criteria.

NSTEMI usually results from severe coronary artery narrowing, transient occlusion, or microembolization of thrombus and/or atheromatous[2] material. NSTEMI is defined by an elevation of cardiac biomarkers[3] in the absence of ST elevation. The syndrome is termed UA in the absence of elevated cardiac enzymes and ST elevation.

History, physical examination, ECG, biomarkers, ECHO all remain important tools to make an appropriate diagnosis. The management of ACS should focus on rapid diagnosis, risk stratification, and institution of therapies that restore coronary blood flow and reduce myocardial ischemia.

PROBLEM STATEMENT:

Coronary heart disease (CHD) is the leading cause of death in India and the leading cause of death worldwide.[4] Previously thought to affect primarily high-income countries, CHD now leads to more death and disability in low- and middle-income countries, such as India, with the rates that are increasing disproportionately compared to high-income countries. With the epidemiologic transition[5], the Cardio vascular disease (CVD) burden continues to rise in developing countries including India. The projected rise in disease burden due to CVD is expected to make it the prime contributor of total mortality and morbidity.

The distribution and prevalence of CHD in India:

[Indian Atlas of CHD in India (Gupta, 2008)][6]

In 2000, there were an estimated 29.8 million people with CHD in India, out of a total estimated population of 1.03 billion people, or a nearly 3% overall prevalence. (Gupta, 2008, India Census, 2001)[7]. Unadjusted CHD rates have ranged from 1.6% to 7.4% in rural populations and 1% to 13.2% in urban populations. (Gupta, 2008)[8]

CHD prevalence appears to be worsening in India. In developed countries, ischemic heart disease is predicted to rise 30-60% between 1990 and 2020. In developing countries, rates are predicted to increase by 120% in women and 137% in men from 1990 to 2020. (Murray, 1997) Sixty percent of the world's patients with heart disease, including CHD, are predicted to live in India by 2010. (Ghaffar, 2004)[9]. Demographic and health transitions, gene-environmental interactions and early life influences of fetal malnutrition are the likely causes of increased CVD burden in India

CHD affects Indians with greater frequency and at a younger age than counterparts in developed countries,as well as many other developing countries thereby having a greater economic impact on low- and middle-income countries. Age-standardized CVD death rates in people 30-69 years old are 180 per 100,000 in Britain, 280 per 100,000 in China, and 405 per 100,000 in India.[10] Also, 50% of CHD-related deaths in India occur in people <70 years of age, whereas only 22% of CHD-related deaths in Western countries occur in this age group. (Gaziano, 2006)

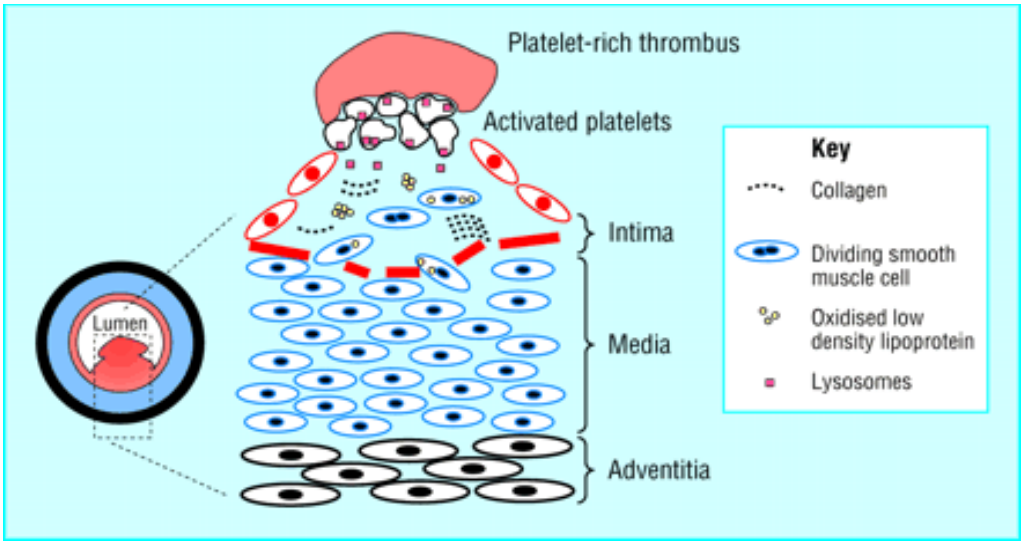
Mortality Associated with CHD:

Almost 2.6 million Indians are predicted to die due to coronary heart disease (CHD), which constitutes 54.1% of all CVD deaths in India by 2020.

PATHOGENESIS:

The process central to the initiation of an acute coronary syndrome is disruption of an atheromatous plaque[11]. Fissuring or rupture of these plaques and consequent exposure of core constituents such as lipid, smooth muscle, and foam cells leads to the local generation of thrombin and deposition of fibrin.

This in turn promotes platelet aggregation and adhesion and the formation of intracoronary thrombus.



Plaque disruption exposes substances that promote platelet activation and aggregation, thrombin generation, and ultimately thrombus formation. The resultant thrombus interrupts blood flow and leads to an imbalance between oxygen supply and demand and, if this imbalance is severe and persistent, to myocardial necrosis.[12]

When plaque disruption occurs, a sufficient quantity of thrombogenic substances is exposed, and the coronary artery lumen may become obstructed by a combination of platelet aggregates, fibrin, and red blood cells that may produce an extensive thrombus filling a large segment of the infarct-related artery. An adequate collateral network that prevents necrosis from occurring can result in clinically silent episodes of coronary occlusion. Disruption of plaques is now considered to underlie most acute coronary syndromes (ACS).

STEMI:

HISTORY AND PHYSICAL EXAMINATION:

Symptoms

The classic symptom of MI is precordial or retrosternal discomfort that is commonly described as a pressure, crushing, aching, or burning sensation. Radiation of the discomfort to the neck, back, or arms frequently occurs, and the pain is usually persistent. The discomfort typically achieves maximum intensity over several minutes and can be associated with nausea, diaphoresis, generalized weakness, and a fear of impending death. Some patients,

particular the elderly, may also present with syncope, unexplained nausea and vomiting, acute confusion, agitation, or palpitations.[13]

Approximately 20 percent of MI patients are asymptomatic or have atypical symptoms that are not initially recognized. Painless myocardial infarction occurs more frequently in the elderly, women, diabetics, and postoperative patients. These patients tend to present with dyspnea or frank congestive heart failure as their initial symptom.

Physical Examination

Patients can appear anxious and uncomfortable. Those with substantial left ventricular (LV) dysfunction at presentation may have tachycardia, pulmonary rales, tachypnea, and a third heart sound. The presence of a mitral regurgitant murmur suggests ischemic dysfunction of the mitral valve apparatus, rupture, or ventricular remodeling.

In patients with right ventricular infarction, increased jugular venous pressure, Kussmaul sign (rise in jugular venous pressure with inspiration), and a right ventricular third sound may be present.[14] Such patients virtually always have inferior infarctions, usually without evidence of left-heart failure, and may have exquisite blood pressure sensitivity to nitrates or hypovolemia. In patients with extensive left ventricular dysfunction, shock is indicated by

hypotension, diaphoresis, cool skin and extremities, pallor, oliguria, and possible confusion[15].

DIAGNOSIS:

Revised Definition of Myocardial Infarction (MI)[16]

Criteria for Acute, Evolving, or Recent MI

Either of the following criteria satisfies the diagnosis for acute, evolving, or recent MI:

1. Typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of the following:

a) Ischemic symptoms

b) Development of pathological Q waves in the ECG

c) ECG changes indicative of ischemia (ST segment elevation or depression)

d) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

2. Pathological findings of an acute myocardial infarction

Biomarkers:

Cardiac troponin (CTn) is the biomarker of choice because it is the most sensitive and specific marker of myocardial injury/ necrosis available.

Troponin levels usually increase after 3-4 hours. If the first blood sample for CTn is not elevated, a second sample should be obtained after 6-9 h, and sometimes a third sample after 12 to 24 hours is required. Troponin level may remain elevated up to 2 weeks. Elevated CTn values signal a higher acute risk and an adverse long term prognosis. Creatine Kinase MB is less sensitive and specific for the diagnosis of NSTE ACS. However, it remains useful for the diagnosis of early infarct extension (reinfarction) and peri-procedural MI because of its short half life. NT-Pro BNP is helpful in assessing left ventricular failure patients.[17]

Biomarkers for the Evaluation of Patients with ST-Elevation Myocardial Infarction

Biomarker	Molecular Weight (D)	Range of Times to Initial Elevation (hr)	Mean Time to Peak Elevations (Nonreperfused)	Time to Return to Normal Range
MB-CK	86,000	3–12	24 hr	48-72 hr
cTnI	23,500	3–12	24 hr	5-10 d
cTnT	33,000	3–12	12 hr-2 d	5-14 d

Electrocardiogram:

Characteristically, completely occlusive thrombi in case of STEMI lead to a large zone of necrosis involving the full or nearly full thickness of

the ventricular wall in the myocardial bed subtended by the affected coronary artery and typically produce ST elevation on the ECG. Infarction alters the sequence of depolarization ultimately reflected as changes in the QRS. The most characteristic change in the QRS that develops in the majority of patients initially presenting with ST elevation is the evolution of Q waves in the leads overlying the infarct zone—leading to the term Q-wave infarction. In the minority of patients presenting with ST elevation, no Q waves develop, but other abnormalities of the QRS complex are frequently seen, such as diminution in R wave height and notching or splintering of the QRS.[17]

The infarction process evolves through three easily recognizable electrocardiographic phases. These three phases and their characteristic ECG manifestations are as fallows[18];

1. The hyperacute phase:
    a) Increased ventricular activation time.
    b) Increased R wave amplitude.
    c) Slope ST segment elevation.
    d) Tall and widened T waves.
2. The fully evolved phase:
    a) A Qs or Qr complex, loss of R wave amplitude.
    b) Coved ST segment elevation.
    c) Symmetrical, pointed T wave inversion.

3. The chronic stabilized phase:

a) Prominent Q waves.

b) Isoelectric ST segment.

c) Upright T wave.

Localization of infarction:

Infarction of the left ventricle;

a) The anterior wall.

b) The inferior wall.

c) The posterior wall.

Infarction of the right ventricle;

Echocardiography:

Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality is useful for the diagnosis particularly in patients with typical anginal pain but without ECG evidence of MI.[19] Echocardiography and Doppler examination should be done after hospitalization to assess the global left ventricular function and any regional wall motion abnormality.

PROGNOSIS ASSESSMENT:

Killip Classification[20] for Patients with ST-Segment Elevation Myocardial Infarction

Killip class	Hospital mortality (%)
I No congestive heart failure	6
II Mild congestive heart failure, rales, S_3, congestion on chest radiograph	17
III Pulmonary edema	38
IV Cardiogenic shock	81

APPROACH TO MANAGEMENT:

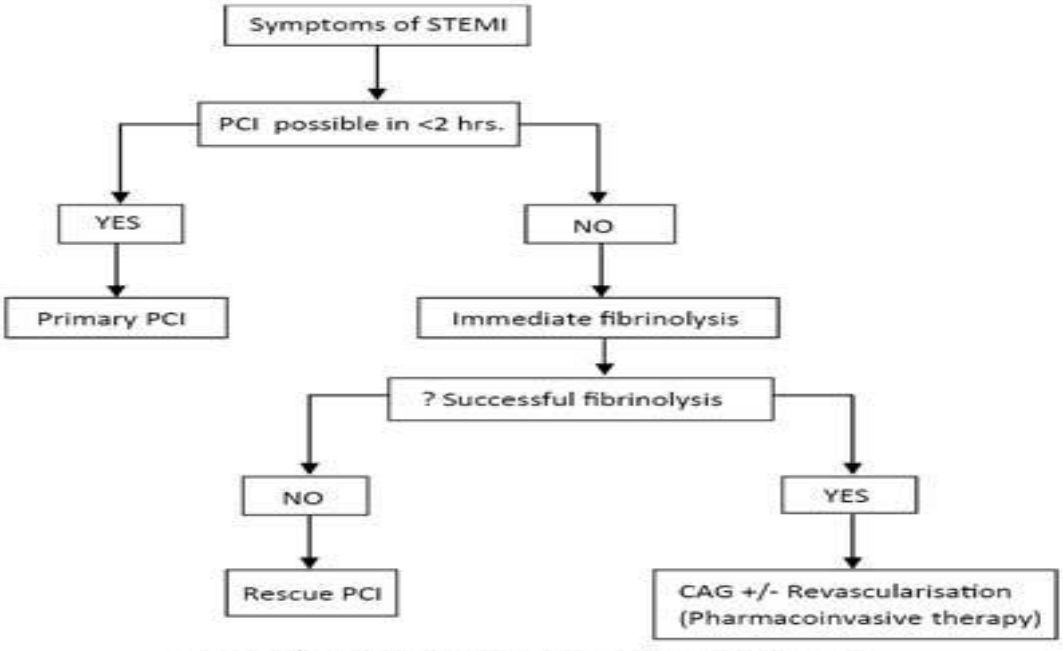


Fig. 3 : Approach to Management of STEMI

Initial Therapy in the Emergency Department:

The initial management of patients in the emergency department includes the use of oxygen, aspirin, beta blockers, analgesia, nitroglycerin, and anticoagulation with heparin.[21]

Reperfusion Strategies

The main goal of STEMI management is rapid reperfusion to establish coronary blood flow to ischemic myocardium. Currently, there are three main reperfusion strategies[22]: thrombolytic therapy, primary PCI, and thrombolytic-facilitated primary PCI.

UA and NSTEMI:

HISTORY AND PHYSICAL EXAMINATION:

Symptoms:

The typical clinical presentation of NSTE ACS is retro sternal pressure or heaviness ("angina") radiating to the left arm, neck or jaw which may be intermittent (usually lasting several minutes) or persistent. There are several atypical symptoms and these include epigastric pain, recent onset indigestion, stabbing chest pain and are often observed in younger and older patients, in women, and in patients with diabetes.

The following clinical presentations are usually included in unstable angina,[23]

- Prolonged (> 20 min) anginal pain at rest.
- New onset (de novo) severe angina (class III of the classification of Canadian Cardiovascular Society (CCS).
- Recent destabilization of previously stable angina with at least CCS III angina characteristics (crescendo angina) or
- Post MI angina.

Physical examination:

The clinical examination is frequently normal. The presence of tachycardia, heart failure or haemodynamic instability must prompt the physician to expedite the diagnosis and treatment of patients. It is important to identify clinical circumstances that may precipitate or exacerbate NSTE-ACS, such as anemia, infection, fever and metabolic or thyroid disorders. An important goal of physical examination is to exclude non-cardiac causes of chest pain and non-ischemic cardiac disorders (e.g. pulmonary embolism, aortic dissection, pericarditis, valvular heart disease) or extra cardiac causes.

DIAGNOSIS:

Electrocardiogram:

In NSTE ACS, ECG may show ST segment deviation, T wave changes or may remain normal. In several studies, around 5% patients with normal

ECG who were discharged from the emergency department were ultimately found to have acute MI or UA. ST segment shifts and T wave changes are the ECG indicators of unstable CAD. The number of leads showing ST depression and the magnitude of ST depression are indicative of the extent and severity of ischemia and correlate with the prognosis. ST depression of > 2 mm carries an increased mortality risk. Inverted T waves, especially if marked (greater than or equal to 2mm (0.2 mv) also indicate UA/ NSTEMI. Q waves suggesting prior MI indicate a high likelihood of IHD.

Biomarkers:

Cardiac troponin (CTn) is the biomarker of choice because it is the most sensitive and specific marker of myocardial injury/ necrosis available. Creatine Kinase MB is less sensitive andspecific for the diagnosis of NSTE ACS. However, it remains useful for the diagnosis of early infarct extension (reinfarction) and peri-procedural MI because of its short half life. NT-Pro BNP is helpful in assessing left ventricular failure patients. Biomarkers will be negative in UA.

Echocardiography:

Echocardiography and Doppler examination should be done after hospitalization to assess the global left ventricular function and any regional wall motion abnormality. Echocardiography also helps in excluding other causes of chest pain.

PROGNOSIS ASSESSMENT:

NSTE ACS includes a heterogeneous group of patients with a highly variable prognosis. The risk stratification is necessary for prognosis assessment and treatment. A simple TIMI risk score11 has been validated and can be used.A TIMI score <3 usually indicates a low risk and a TIMI score = 3-4 indicates intermediate risk, where as score of 5-7 is high risk.

In general, patients having multiple coronary risk factors, advanced age, rest angina, clinical left ventricular (LV) dysfunction, prior history of percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABGS) or patients with dynamic ST-T changes and elevation of troponin or CK-MB indicates myocyte necrosis and a high risk. There are other risk models based on PURSUIT trial and GRACE registry.

THE TIMI RISK [24]SCORE FOR Non STEMI

Characteristics	**score**
History: Age > 65 yrs.	1
>3 risk factor for CAD	1
(DM, HT, Dyslipidemia, Family h/O	
Known CAD	1
H/O aspirin in last 7 days	1
Presentation	
2 anginal events < 24 hrs	1
ST deviation > o.5 mm	1
Elevated cardiac enzymes	1
RISK SCORE TOTAL	0-7

APPROACH TO MANAGEMENT:

The aims of therapy for UA/NSTEMI patients are to control symptoms and prevent further episodes of myocardial ischemia and/or necrosis. Beta blockers, nitrates, and, to a lesser extent, calcium channel blockers reduce the risk of recurrent ischemia. Revascularization eliminates ischemia in many patients.

Hospitalized moderate- to high-risk ACS patients should be treated with aspirin (ASA), clopidogrel, antithrombin therapy, a beta blocker, statin, and, in selected individuals, a GPIIb/IIIa inhibitor. Furthermore, critical decisions are required regarding the angiographic strategy. One option, commonly termed the early invasive strategy, incorporates an angiographic[25] approach in which coronary angiography and revascularization are performed unless a contraindication exists. The alternative approach is the early conservative strategy with angiography reserved for patients with recurrent ischemia at rest or a high-risk noninvasive evaluation for ischemia.

Regardless of the angiographic strategy, an assessment of LV function should be strongly considered. When coronary angiography is not scheduled, the patient is evaluated at rest and/or with stress for inducible myocardial ischemia or LV systolic dysfunction

SECONDARY PREVENTION:

Modifiable Risk Factors for the

Prevention of Cardiovascular Disease[26]

This is most important to prevent further episodes of ACS thereby reducing the morbidity and mortality.

Class 1 risk factors & intervention:

Smoking	–	Cessation of smoking strongly advocated as this will result in 60% reduction in CHD risk by three years.
Dyslipidemia	–	Dietary changes combined with statins strongly recommended.
Hypertension	-	Dietary advice , anti hypertensive agents
Aspirin in secondary prevention	-	following MI
Beta blockers	-	**following MI**
ACE inhibitors	-	Following MI, LV dysfunction

Class 2 risk factors & intervension:

Diabetes	-	Dietary advice, exercise, Drugs
Obesity	-	Weight reduction, life style modification Moderate alcohol consumption

Class 3 risk factors and interventions are currently under active investigation Menopause, hormone replacement, Dietary supplements, Psychological factors, Novel biochemical and genetic markers (fibrinogen, homocysteine, Lp(a) etc.) Additional observational data needed to clarify role of these factors in clinical practice.

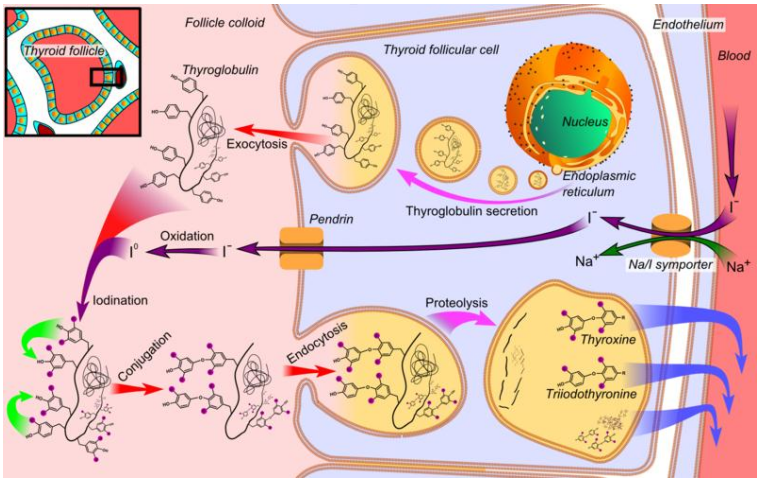
THYROID

The thyroid gland produces two important hormones, thyroxine (T4) and triiodothyronine (T3)[27.] Acting through nuclear receptors, these hormones play a critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult. T_3 and T_4 are synthesized from both iodine and tyrosine. The thyroid also produces calcitonin, which plays a role in calcium homeostasis.

Thyroid Hormone Synthesis, Metabolism, and Action

Thyroid Hormone Synthesis:

Thyroid hormones are derived from thyroglobulin, a large iodinated glycoprotein. After secretion into the thyroid follicle, Tg is iodinated on tyrosine residues that are subsequently coupled via an ether linkage. Reuptake of Tg into the thyroid follicular cell allows proteolysis and the release of newly synthesized T_4 and T_3.



Steps in thyroid hormone synthesis

1) Iodide uptake:

Iodide uptake is a first step in thyroid hormone synthesis. Ingested iodine is bound to serum albumin. The thyroid gland extracts iodine from the circulation. Iodide uptake is mediated by the Na^{+}/I^{-} symporter (NIS), which is expressed at the basolateral membrane of thyroid follicular cells. NIS is most highly expressed in the thyroid gland. The iodide transport mechanism is highly regulated, allowing adaptation to variations in dietary supply. The selective expression of NIS in the thyroid allows isotopic scanning, treatment of hyperthyroidism, and ablation of thyroid cancer with radioisotopes of iodine, without significant effects on other organs. Mutation of the NIS gene is a rare cause of congenital hypothyroidism, underscoring its importance in thyroid hormone synthesis. Another iodine transporter, pendrin, is located on the apical surface of thyroid cells and mediates iodine efflux into the lumen. Mutation of the PENDRIN[28] gene causes Pendred syndrome, a disorder characterized by defective organification of iodine, goiter, and sensorineural deafness. The recommended average daily intake of iodine is 150 g/d for adults, 90–120 g/d for children and 200 g/d for pregnant women. Urinary iodine is >10 g/dL in iodine-sufficient populations.

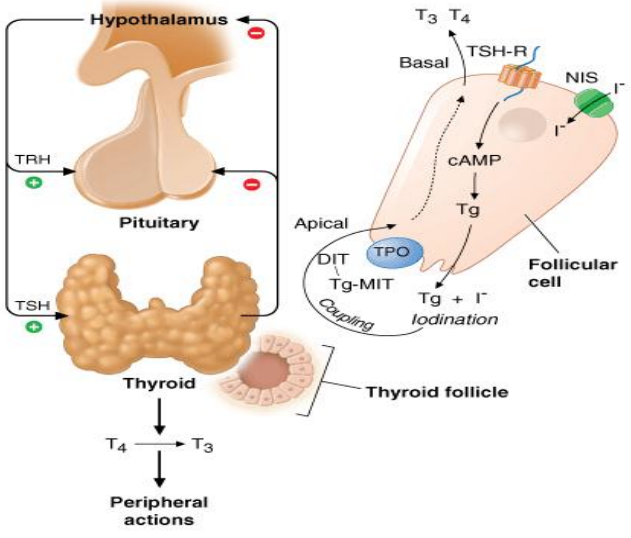
2) Organification:

After iodide enters the thyroid, it is trapped and transported to the apical membrane of thyroid follicular cells, where it is oxidized in an organification reaction that involves TPO and hydrogen peroxide. The reactive iodine atom is added to selected tyrosyl residues within Tg, a large (660 kDa) dimeric protein that consists of 2769 amino acids[30]

3) Coupling: The iodotyrosines in Tg are then coupled via an ether linkage in a reaction that is also catalyzed by TPO. Either T_4 or T_3 can be produced by this reaction, depending on the number of iodine atoms present in the iodotyrosines.

4) Storage: The synthesized hormones stored in the follicle.

5) Release: Tg is taken back into the thyroid cell, where it is processed in lysosomes to release T_4 and T_3.



Regulation of the thyroid hormone synthesis

TSH, secreted by the thyrotrope cells of the anterior pituitary, plays a pivotal role in control of the thyroid axis and serves as the most useful physiologic marker of thyroid hormone action. The extent and nature of carbohydrate modification are modulated by thyrotropin-releasing hormone (TRH) stimulation and influence the biologic activity of the hormone.

The thyroid axis is a classic example of an endocrine feedback loop. Hypothalamic TRH stimulates pituitary production of TSH, which, in turn, stimulates thyroid hormone synthesis and secretion. Thyroid hormones feed back to inhibit TRH and TSH production. The "set-point" in this axis is established by TSH. TRH is the major positive regulator of TSH synthesis and secretion. TSH is measured using immunoradiometric assays[31] that are highly sensitive and specific. These assays readily distinguish between normal and suppressed TSH values; thus, TSH can be used for the diagnosis of hyperthyroidism (low TSH) as well as hypothyroidism (high TSH).

Other Factors that Influence Hormone Synthesis and Release:

Although TSH is the dominant hormonal regulator of thyroid gland growth and function, a variety of growth factors, most produced locally in the

thyroid gland, also influence thyroid hormone synthesis. These include insulin-like growth factor I (IGF-I), epidermal growth factor, transforming growth factor (TGF-), endothelins, and various cytokines.

Thyroid Hormone Transport and Metabolism:

T_4 is secreted from the thyroid gland in about twentyfold excess over. T_3. Both hormones are bound to plasma proteins, including thyroxine-binding globulin (TBG); transthyretin (TTR), and albumin. The plasma-binding proteins increase the pool of circulating hormone, delay hormone clearance, and may modulate hormone delivery to selected tissue sites. The concentration of TBG is relatively low (1–2 mg/dL), but because of its high affinity for thyroid hormones (T_4 > T_3), it carries about 80% of the bound hormones. Albumin has relatively low affinity for thyroid hormones but has a high plasma concentration (~3.5 g/dL), and it binds up to 10% of T_4 and 30% of T_3. TTR carries about 10% of T_4 but little T_3. When the effects of the various binding proteins are combined, approximately 99.98% of T_4 and 99.7% of T_3 are protein-bound.

Because T_3 is less tightly bound than T_4, the fraction of unbound T_3 is greater than unbound T_4, but there is less unbound T_3 in the circulation because it is produced in smaller amounts and cleared more rapidly than T_4. The unbound, or free, concentrations of the hormones are ~2 x 10^{-11}M for T_4

and ~6 x 10^{-12}M for T_3, which roughly correspond to the thyroid hormone receptor binding constants for these hormones. The unbound hormone is thought to be biologically available to tissues.

Deiodinases

T_4 may be thought of as a precursor for the more potent T_3. T_4 is converted to T_3 by the deiodinase enzymes. Type I deiodinase, which is located primarily in thyroid, liver, and kidney, has a relatively low affinity for T_4. Type II deiodinase has a higher affinity for T_4 and is found primarily in the pituitary gland, brain, brown fat, and thyroid gland. Expression of type II deiodinase allows it to regulate T_3 concentrations locally, a property that may be important in the context of levothyroxine (T_4) replacement. Type II deiodinase is also regulated by thyroid hormone; hypothyroidism induces the enzyme, resulting in enhanced T_4 T_3 conversion in tissues such as brain and pituitary. T_4 T_3 conversion is impaired by fasting, systemic illness or acute trauma, oral contrast agents, and a variety of medications (e.g., propylthiouracil, propranolol, amiodarone, glucocorticoids).[32] Type III deiodinase inactivates T_4 and T_3 and is the most important source of reverse T_3 (rT_3). Massive hemangiomas that express type III deiodinase are a rare cause of hypothyroidism in infants.

THYROID HORMONE ACTION:

Thyroid Hormone Transport

Circulating thyroid hormones enter cells by passive diffusion and via the monocarboxylate 8 (MCT8) transporter. After entering cells, thyroid hormones act primarily through nuclear receptors.

Physiological effects of thyroid hormones:

Heart	**:**	Increases number of β adrenergic receptors and enhances response to catecholamines
Adipose tissue	**:**	Stimulate lipolysis
Muscle	**:**	Increases protein breakdown
Bone	**:**	Promote growth and development
Nervous system	:	Promote normal brain development
Gut	:	Increases carbohydrate absorption
Lipoprotein	:	Stimulate LDL receptors
Others	**:**	Increases metabolic rate and oxygen consumption

SICK EUTHYROID SYNDROME:

Definition:

Disturbances in the circulating concentrations of thyroid hormones and TSH assays arising in systemic non-thyroid illnesses without preexisting hypothalamic-pituitary- thyroid gland dysfunction and normalizing after recovery.[34]

Classification

- Low serum T_3, normal T_4. The most common biochemical abnormality, it is seen in approximately 70% hospitalized patients. T_3 reduced by about 50%, rT_3increased (except in renal failure) due to its decreased clearance as a result of reduced activity/production of 5′ mono-deiodinase Type 1.
- Low serum total T_3 and T_4. Usually seen in severely ill patients. Free T_4 is normal owing to inhibition of T_4 binding or production of altered TBG.
- High serum total T_4, normal total T_3. Seen in patients with liver disease producing increased quantities of TBG. Free T_3 low or low-normal, rT_3 high.
- Increased serum total-T_4 and TBG, normal T_3 and paradoxical decreases in rT_3. Seen in patients with HIV infection.

Clinical considerations

- Drugs, used to treat the severely ill, affect thyroid physiology and these factors to be excluded before diagnosing SES.

Drugs and the thyroid gland

Drugs can alter thyroid hormone status by affecting thyroid hormone synthesis, transport or metabolism[35]. They act at a number of sites to:

- Block I^- uptake, e.g. lithium.
- Decrease iodination of the tyrosine molecules in thyroglobulin, e.g. some sulfonamides and sulfonylureas.
- Inhibit hormone secretion, e.g. lithium

Alter thyroid binding globulin concentration and, thus, concentrations of 'free' thyroid hormones, e.g. estrogens, clofibrate increase TBG whilst androgens, glucocorticoids and L-asparginase decrease TBG.

- Alter binding to TBG or transthyretin, e.g. salicylates, phenytoin and some non-steroidal anti-inflammatories such as fenclofenac.
- Decrease conversion of T_4 to T_3, e.g. glucocorticoids, propranolol, amiodarone, some iodinated radiographic contrast agents.
- Increase hormone degradation or excretion, e.g. phenytoin, carbamazepine, cholestyramine.

The most prominent alterations are low serum triiodothyronine (T3) and elevated reverse T3 (rT3), leading to the general term "low T3 syndrome."

Thyroid-stimulating hormone (TSH), thyroxine (T4), free T4 (FT4), and free T4 index (FTI) also are affected in variable degrees based on the severity and duration of the SES. As the severity of the SES increases, both serum T3 and T4 levels drop and gradually normalize as the patient recovers[36].

Sick Euthyroid State is observed in most of the acute and chronic illnesses. Examples of illness include the following:

- Sepsis
- Burns
- CVD
- Gastrointestinal diseases
- Pulmonary diseases
- Renal diseases
- Surgery
- Malignancy
- Bone marrow transplantation

Proposed mechanisms explaining abnormalities in thyroid hormone levels Cytokines:

Cytokines are thought to play a role in NTI—particularly interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)-alpha, and interferon-beta.

Cytokines are thought to affect the hypothalamus, the pituitary, or other tissues, inhibiting production of TSH, thyroid-releasing hormone (TRH), thyroglobulin, T3, and thyroid-binding globulins. Cytokines are also thought to decrease the activity of type I deiodinase and to decrease the binding capacity of T3 nuclear receptors.

Deiodination:

Peripheral deiodination of T4 to T3 is impaired, secondary to decreased activity of type I deiodinase enzyme, which deiodinates T4 to T3. Diminished enzyme activity accounts for decreased deiodination of T4 to T3.

An alternative explanation is that reduced tissue uptake of T4 secondary to deficiency of cytosolic cofactors (eg, nicotinamide adenine dinucleotide phosphate [NADPH], glutathione) results in decreased substrate for type I deiodinase enzyme. Type I deiodinase is a selenoprotein; because selenium deficiency is common in critically ill patients, some propose that selenium deficiency may contribute to type I deiodinase malfunction. Inhibition of thyroid-releasing hormone and thyroid-stimulating hormone secretion: Inhibition of plasma membrane transport of iodothyronines: Thyroxine-binding globulin decrease and desialation: T4-binding globulin (TBG) is a member of the serine protease inhibitors. Diminished T4 in NTI has been proposed to be due to low TBG caused by protease cleavage at inflammatory sites in acute inflammatory conditions[37].

Sick Euthyroid State in ACS:

The low T3 syndrome, the most common type of sick Euthyroid syndrome , once believed to be a beneficial adaptive mechanism under conditions of stress, has emerged as a strong prognostic determinant in chronic systolic heart failure. Increased mortality among patients with low T3 syndrome has also been observed in acute myocardial infarction, a common precursor of chronic heart failure of ischemic origin.

Acute myocardial infarction (AMI) may be associated with a number of endocrine alterations, including those of the SES which reflect the acute hormone response to stress and trauma. A transient decrease in T3 and increase in reverse (r)T3 occurs within the first 24 h, reaching the highest degree on the third day after the attack. The decreased nutrition during the first days of the myocardial infarct, the increased levels of serum cortisol, circulating free fatty acids, free radicals, cytokines are some of the factors which may contribute to the 50-monodeiodinase inhibition. Less prominent are the alterations of T4 and thyrotropin (TSH) which appear to be non-significantly changed in most of the patients with acute myocardial infarct. It is known from several studies that several cytokines can be found elevated in patients with cardiac ischemia or AMI.[39] From *in vitro* studies it is of particular interest that ischemic myocytes produce cytokines such as interleukin-6 (IL-6) and its synthesis is accelerated by reperfusion.

Interleukin-6 seemed to be an important cytokine produced by the injured myocytes in patients with AMI, and strong negative correlation between serum IL-6 concentration and left ventricular ejection fraction (LVEF) has been demonstrated. Similar observations have been made by studying tumor necrosis factor-a (TNF-a), IL-1a and soluble IL-2 receptor (sIL-2-R) which were found to be significantly elevated in AMI, with the highest levels noted in the most severe and complicated cases of myocardial infarction[40].

In addition, there is a gradual progression from a low T3 level to an advanced illness with extremely low T3 and T4 levels, which can be associated with high mortality. Similarly excessive decreases of T4 are linked with increasing mortality in AMI. There several studies support the idea that excessive decreases of T4 are linked with seriousness of AMI.

MATERIALS AND METHODS

The present study titled ***"Thyroid Profile in Acute coronary syndrome"*** was carried out in the Department of Medicine and in the Department of cardiology, kilpauk medical college and hospital (Chennai).

Study design : Cross sectional study.

Period of study: November 2010 to October 2011.

Materials :

Questionnaire, BMI calculation, Blood pressure, TIMI score and Killip's class, CBC, CRP, FBS and PPBS, Blood Urea, Serum creatinine and electrolytes, Urinalysis, serial ECGs, Chest X ray, Fasting lipid profile, Thyroid profile (T3, T4, FT3, FT4, TSH and rT3) and echocardiography.

Study group :

The study group included 155 patients who were admitted in ICCU with the diagnosis of acute coronary syndrome.

Inclusion criteria

Patients with acute coronary syndrome (STEMI/ NSTEMI/ UA) irrespective of their gender, race, ethnic group, age, and clinical severity.

Exclusion criteria

- Patients with known CHD with or without LV dysfunction
- Patients with known thyroid disease
- Patients with TSH level of <0.4 and > 4.0 μ IU/ml .
- Patients who had received iodinated contrast agent within the last two weeks.
- Patients with chronic renal failure
- Patients with chronic obstructive pulmonary disease exacerbation
- Patients with acute illness (sepsis, DKA, severe respiratory failure, and recent H/O surgery)
- Patients with hepatic dysfunction and/ or cirrhosis
- Patients using drugs interfering with thyroid function (amiodarone, propranolol, corticosteroids and oral contraceptives)

METHODS

One hundred and fifty five patients admitted during November2010 to October 2011 in ICCU, KMC Hospital were prospectively studied. All patients in the study group were selected irrespective of their age gender, race, ethnic group, and clinical severity. A complete history was recorded to fulfill the exclusion criteria and risk factors for CHD were noted. A thorough physical examination was done. Risk stratification was done using TIMI score and Killips classes. Blood samples were taken. Echocardiography was done in all patients.

Investigations:

12 lead ECGs were taken serially.

Complete blood count :

RBC count:

TC : DC:

Platelet count

Hb in gm%

ESR

CRP:

Agar-Gel Precipitin-Inhibition Technique was used for estimation.

Urine analysis:

Sugar, albumin, deposits.

Blood sugar:

FBS and PPBS are estimated by Trinder's (Glucose oxidase) method and read at 505/670 nm.

Renal function test:

Blood urea was estimated using DAM method (Diacetyl Monoxime). Serum creatinine was estimated using Modified Jaffe's method. Serum electrolytes were estimated using flame photometry with ion specific electrodes.

Fasting lipid profile: Methods used were,

For, T. Chol. - CHOD POD METHOD

HDL - Selective immune precipitation method

TGL - Enzymatic calorimetric method

LDL - Derived from TC and TGL values.

VLDL - Derived from triglyceride values

CPK - MB, was measured by Column Chromatography.

Fasting thyroid profile:

TSH was estimated using Ultrasensitive sandwich chemi luminescent immuno assay.

T_4, T_3, FT_4 and FT_3 were measured by Competitive chemi luminescent immuno assay reverse T3 was measured by radioimmunoassay, using the Serono kit.

Echocardiography was done to look for wall motion abnormalities and to assess LV function.

DEFINITIONS

Acute coronary syndrome:

a) Criteria for Acute, Evolving, or Recent MI

Either of the following criteria satisfies the diagnosis for acute, evolving, or recent MI:

1. Typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of the following:

a) Ischemic symptoms

b) Development of pathological Q waves in the ECG

c) ECG changes indicative of ischemia (ST segment elevation or depression)

d) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

2) Pathological findings of an acute myocardial infarction

b) Unstable Angina

Prolonged (> 20 min) anginal pain at rest.

New onset (de novo) severe angina (class III of the classification of Canadian Cardiovascular Society (CCS).

Recent destabilization of previously stable angina with at least CCS III angina characteristics (crescendo angina) or Post MI angina

Sick Euthroid Syndrome

Definition: Disturbances in the circulating concentrations of thyroid hormones and TSH assays arising in systemic non-thyroid illnesses without preexisting hypothalamic-pituitary- thyroid gland dysfunction and normalizing after recovery.

Diabetes Mellitus Systemic Hypertension (As per the ADA 2010 Guidelines)

FDS $\geq$ 126mg/dl

PPDS $\geq$ 200 mg/dl

$HBA_1C \geq 6.5$

Subjects on medications for hypertension and those who had a systolic blood pressure of ³ 140 mmHg and / or diastolic blood pressure ³ 90 mmHg were considered to have hypertension.

Dyslipidemia

Adult Treatment Panel III (ATP III) guidelines developed by the National. Cholesterol Education Program have been used to detect

dyslipidemia in the study subjects. Diabetes mellitus is considered as Coronary Heart Disease equivalent. According to the guidelines:

Overweight and Obesity

BMI (WHO criteria for Asian population) is used for classifying the subjects according to the weight status.

BMI Group BMI(kg/m2)

Underweight < 18.5

Normal weight 18.5-22.9

Overweight 23-29.9

Obesity 30.0[4]

Thyroid profile

Reference values:

T3 70 to 100 μg/dl

FT3 : 1.5 to 4.1 pg/ml

FT4 : 0.8 to 1.90 ng/dl

T4 : 4.5 to 12.5 μg/dl

TSH : 0.42 to 5mIU/ml

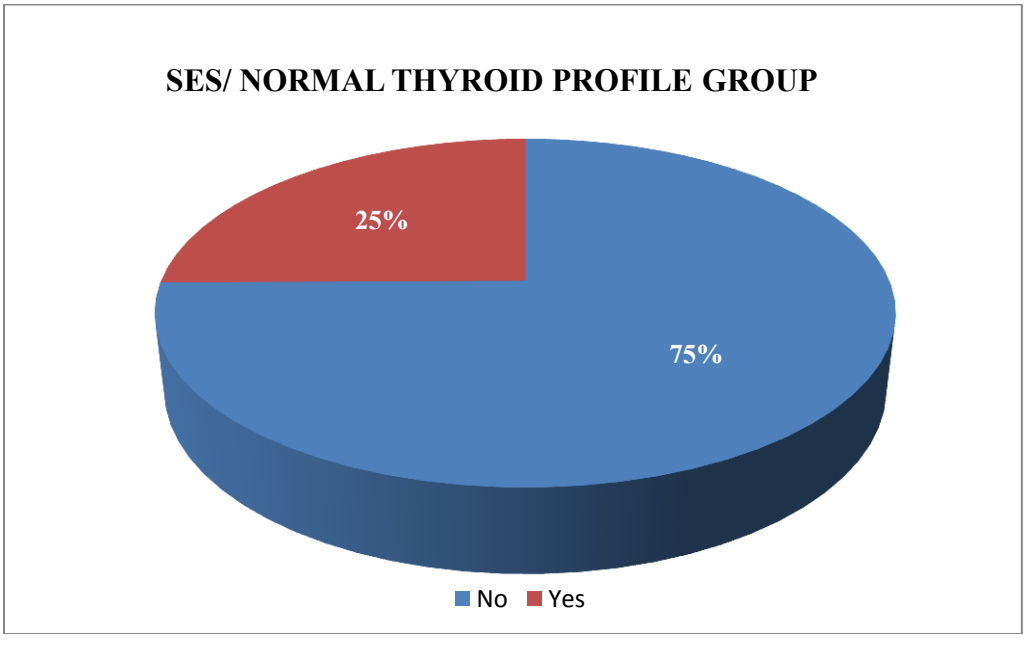
rT3 : 0.09 to 0.35 μg/ml

RESULTS AND ANALYSIS

The present study titled **"Thyroid profile in Acute coronary syndrome"** was undertaken in the Department of Medicine and the Department of Cardiology, kilpauk medical college and hospital (Chennai) over a period of 12 months from November 2010 to October 2011.

I) Prevalence of Sick Euthyroid Syndrome in ACS :

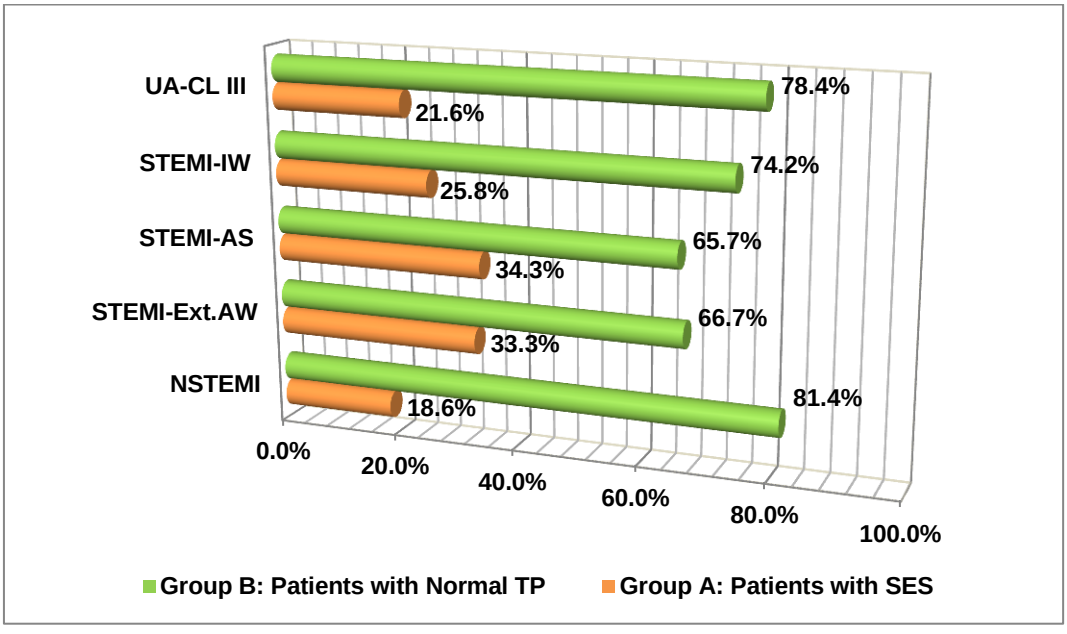
SES	No. of cases	% of cases	Cumulative %
No	116	74.8	74.8
Yes	39	25.2	25.2
Total	**155**	**100.0**	



The above table shows 25.2% (39/155) of patients with Acute Coronary Syndrome had Sick Euthyroid State. Remaining 74.8% (116/155) of ACS patients had normal thyroid profile.

II) Prevalence of Sick Euthyroid State in various Type of ACS

Type of ACS		Patients with SES	Patients with normal Thy Profile	Total
NSTEMI	Count	8	35	43
	% within Type of ACS	18.6%	81.4%	100%
	% within Group	20.5%	30.2%	27.7%
STEMI – AS	Count	3	6	9
	% within Type of ACS	33.3%	66.7%	100%
	% within Group	7.7%	5.2%	5.8%
STEMI-Ext.AW	Count	12	23	35
	% within Type of ACS	34.3%	65.7%	100%
	% within Group	30.8%	19.8%	22.6%
STEMI – IW	Count	8	23	31
	% within Type of ACS	25.8%	74.2%	100%
	% within Group	20.5%	19.8%	20.0%
UA -	Count	8	29	37
	% within Type of ACS	21.6%	78.4%	100%
	% within Group	20.5%	25.0%	23.9%
Total	Count	39	116	155
	% within Type of ACS	25.2%	74.8%	100%
	% within Group	100%	100%	100%



This pie diagram showed,

21.6% (8/37) of patients with Unstable angina had SES;

25.8% (8/31) of patients with STEMI IWMI had SES;

34.3% (12/35) of patients with STEMI ASMI had SES;

33.3% (3/9) of patients with Ext. AWMI had SES;

18.6% (8/43) of patients with NSTEMI had SES.

Chi-Square Tests

	Value	df	P-v alue
Pearson Chi-Square	3.101	4	.541
N of Valid Cases	155		

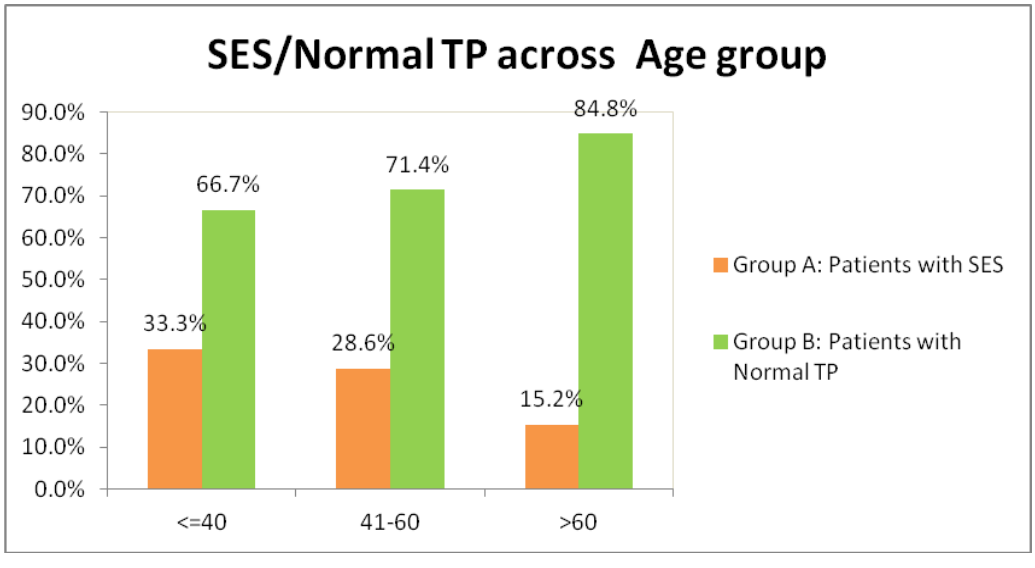
When these values were analyzed with statistical test, there was no significant difference of occurrence of SES with different type of ACS. Hence, the occurrence of SES did not influenced by the type of ACS.

(II) Distribution of Sick Euthyroid Syndrome in ACS patients and Comparison study between Group A (ACS patients with SES) & Group B (ACS patients without SES) :

1) According to age:

Age * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Age	<= 40	Count	6	12	18
		% within Age	33.3%	66.7%	100.0%
		% within Group	15.4%	10.3%	11.6%
	41 - 60	Count	26	65	91
		% within Age	28.6%	71.4%	100.0%
		% within Group	66.7%	56.0%	58.7%
	> 60	Count	7	39	46
		% within Age	15.2%	84.8%	100.0%
		% within Group	17.9%	33.6%	29.7%
Total		Count	39	116	155
		% within Age	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



This chart showed,

33.3% (6/18) of SES patients were less than 40 years of age;

28.6% (26/91) of SES patients were in between 41 and 60 years of age;

15.2% (7/46) of SES patients were more than 60 years of age.

Chi-Square Tests

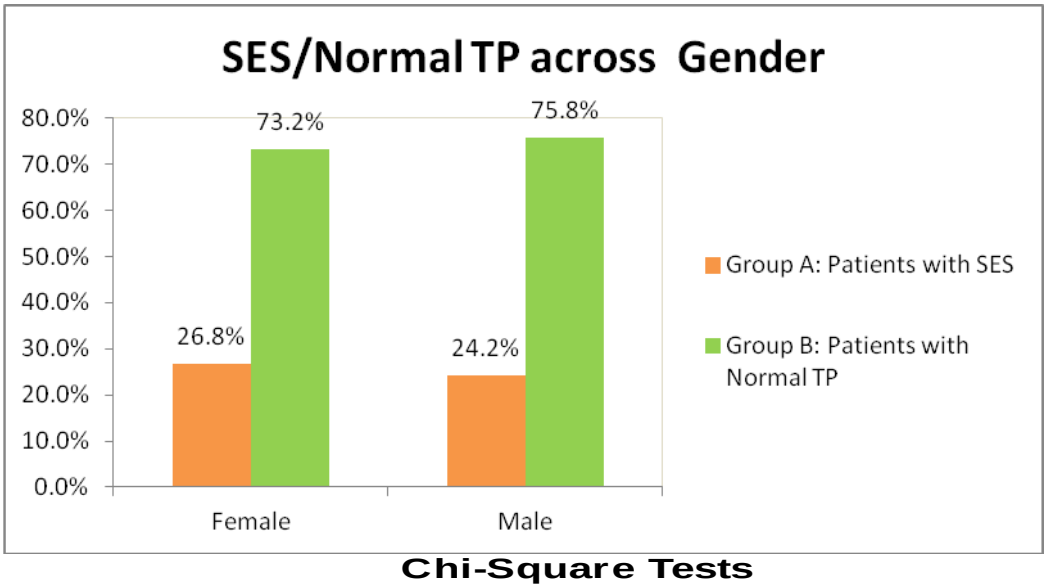
	Value	df	P-value
Pearson Chi-Square	3.616	2	.164
N of Valid Cases	155		

When statistical test was applied, there was no significant difference in the occurrence of SES among different ages. But if we applied the statistical analysis for each age group it was found that there was significant difference in the age group of >60 yrs. The inference is that the occurrence of SES in old age is very less compared to other age groups.

2) According to sex:

SEX * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
SEX	Female	Count	15	41	56
		% within SEX	26.8%	73.2%	100.0%
		% within Group	38.5%	35.3%	36.1%
	Male	Count	24	75	99
		% within SEX	24.2%	75.8%	100.0%
		% within Group	61.5%	64.7%	63.9%
Total		Count	39	116	155
		% within SEX	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

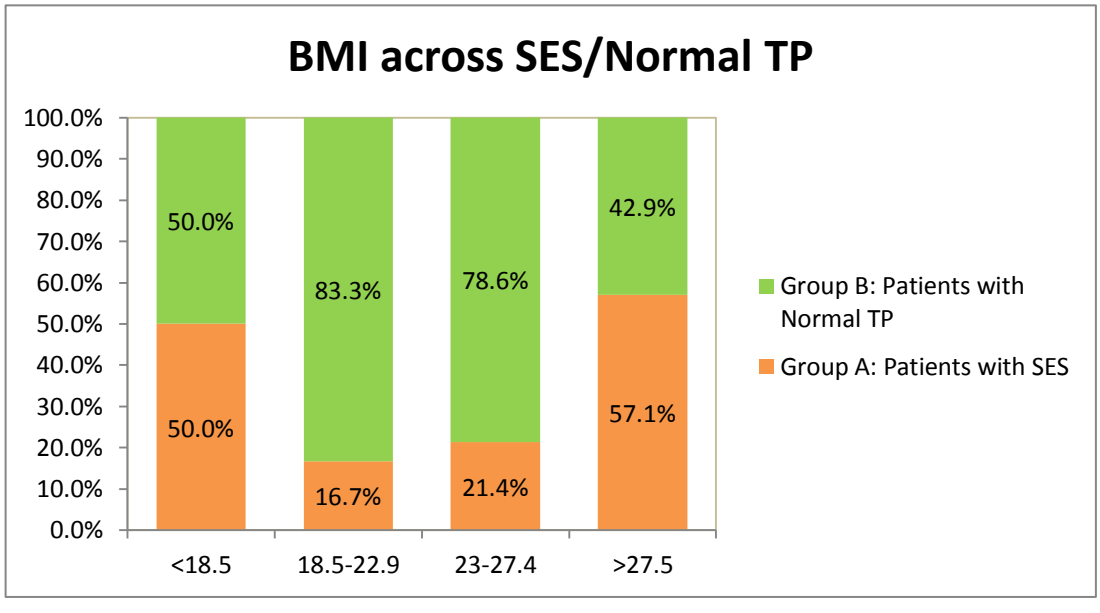
	Value	df	P-value
Pearson Chi-Square	.123	1	.726
N of Valid Cases	155		

P value was > 0.01 i.e. insignificant, the inference is that the occurrence of SES not influenced by sex.

3) According to BMI:

Body Mass Index * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Body Mass Index	< 18.5	Count	1	1	2
		% within Body Mass Index	50.0%	50.0%	100.0%
		% within Group	2.6%	.9%	1.3%
	18.5 - 22.9	Count	8	40	48
		% within Body Mass Index	16.7%	83.3%	100.0%
		% within Group	20.5%	34.5%	31.0%
	23 - 27.4	Count	18	66	84
		% within Body Mass Index	21.4%	78.6%	100.0%
		% within Group	46.2%	56.9%	54.2%
	> 27.5	Count	12	9	21
		% within Body Mass Index	57.1%	42.9%	100.0%
		% within Group	30.8%	7.8%	13.5%
Total		Count	39	116	155
		% within Body Mass Index	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



This bar diagram showed,

57.1% of SES patients were obese { BMI of >27.5}

21.4% of SES patients were overweight { BMI of 23.0 – 27.4 }

16.7% of SES patients had normal { BMI 18.5- 22.9}

Chi-Square Tests

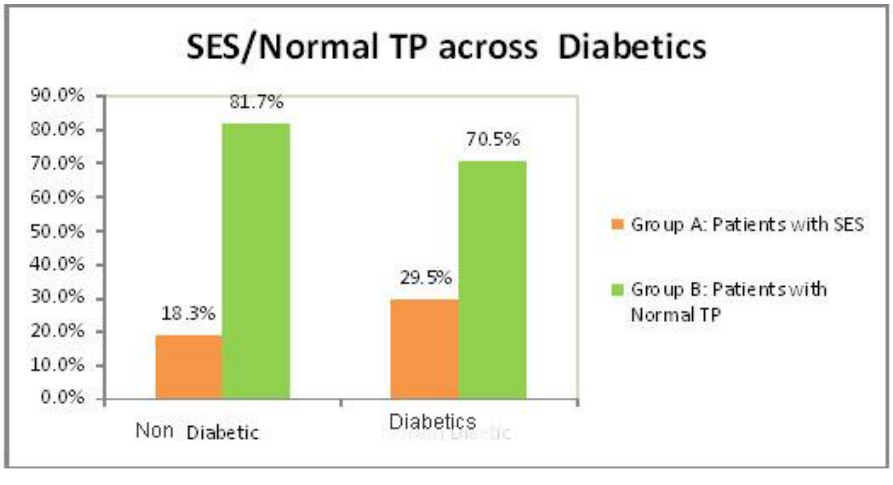
	Value	df	P-value
Pearson Chi-Square	14.523	3	.002
N of Valid Cases	155		

The statistical analysis showed a significant association between the occurrence of SES and High BMI i.e. > 27.5 kg/m2

4) According to Diabetic state:

Diabetics * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Diabetics	No	Count	11	49	60
		% within Diabetics	18.3%	81.7%	100.0%
		% within Group	28.2%	42.2%	38.7%
	Yes	Count	28	67	95
		% within Diabetics	29.5%	70.5%	100.0%
		% within Group	71.8%	57.8%	61.3%
Total		Count	39	116	155
		% within Diabetics	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

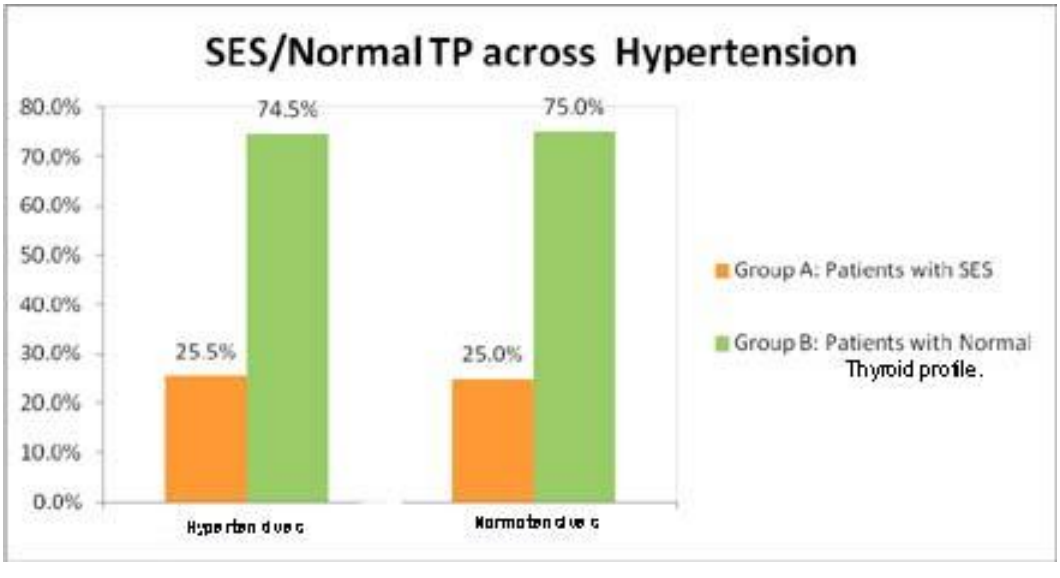
	Value	df	P-value
Pearson Chi-Square	2.424	1	.120
N of Valid Cases	155		

29.5% of diabetics had SES; 18.3% of non diabetics had SES; It was found that this association was statistically not significant.

5) According to Hypertension:

Hypertension * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Hypertension	No	Count	14	41	55
		% within Hypertension	25.5%	74.5%	100.0%
		% within Group	35.9%	35.3%	35.5%
	Yes	Count	25	75	100
		% within Hypertension	25.0%	75.0%	100.0%
		% within Group	64.1%	64.7%	64.5%
Total		Count	39	116	155
		% within Hypertension	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

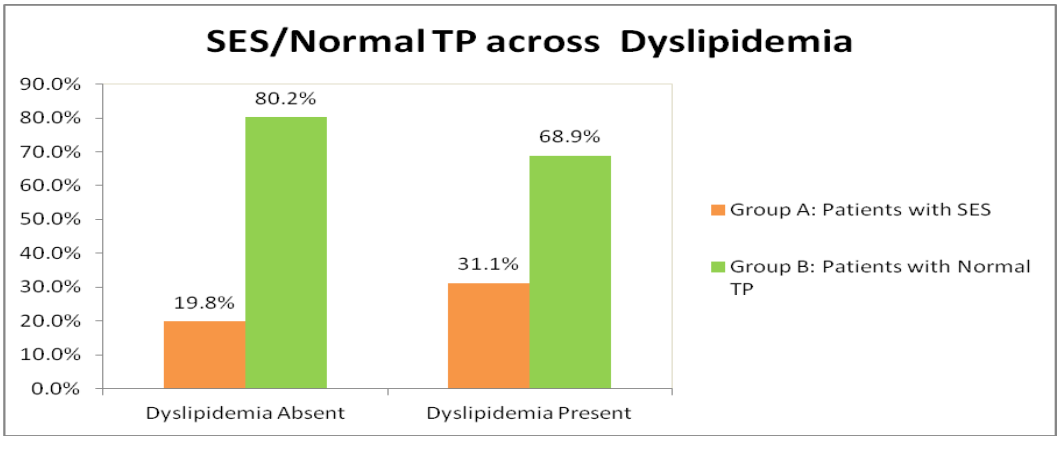
	Value	df	P-value
Pearson Chi-Square	.004	1	.950
N of Valid Cases	155		

25.5% of Hypertensive patients had SES and 25.0% of normotensive patients had SES . This was statistically not significant.

6) According to Dyslipidemia:

Dyslipidemia * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Dyslipidemia	No	Count	16	65	81
		% within Dyslipidemia	19.8%	80.2%	100.0%
		% within Group	41.0%	56.0%	52.3%
	Yes	Count	23	51	74
		% within Dyslipidemia	31.1%	68.9%	100.0%
		% within Group	59.0%	44.0%	47.7%
Total		Count	39	116	155
		% within Dyslipidemia	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

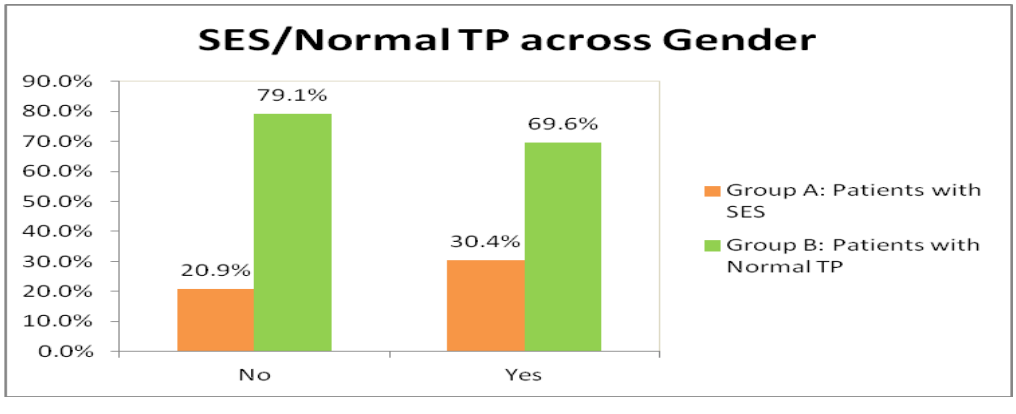
	Value	df	P-value
Pearson Chi-Square	2.635	1	.105
N of Valid Cases	155		

31.1% of patients with dyslipidemia had SES when compared to 19.8% in case of patients with normal lipid profile. This association was statistically not significant.

7) According to smoking habit:

Smoking * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Smoking	No	Count	18	68	86
		% within Smoking	20.9%	79.1%	100.0%
		% within Group	46.2%	58.6%	55.5%
	Yes	Count	21	48	69
		% within Smoking	30.4%	69.6%	100.0%
		% within Group	53.8%	41.4%	44.5%
Total		Count	39	116	155
		% within Smoking	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

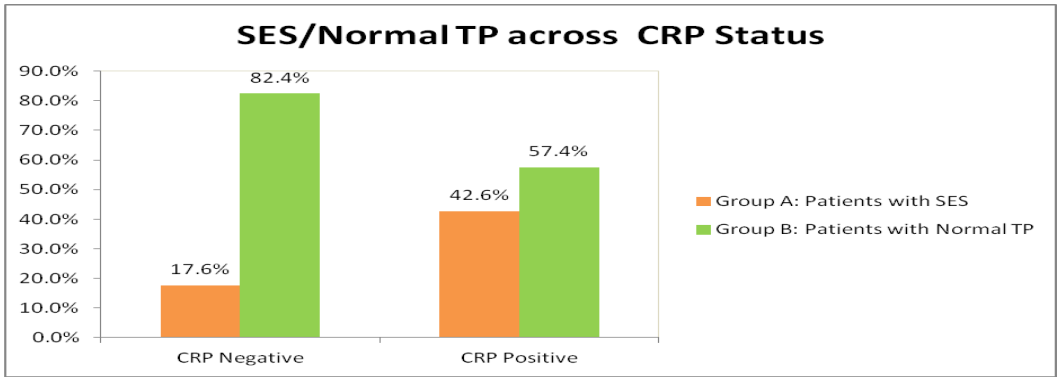
	Value	df	P-value
Pearson Chi-Square	1.837	1	.175
N of Valid Cases	155		

30.4% of smokers had SES when compared to 20.9% in non smokers. P value was >0.01, hence the smoking habit did not influence the prevalence of SES.

8) According to CRP:

CRP Status * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
CRP Status	CRP Negative	Count	19	89	108
		% within CRP Status	17.6%	82.4%	100.0%
		% within Group	48.7%	76.7%	69.7%
	CRP Positive	Count	20	27	47
		% within CRP Status	42.6%	57.4%	100.0%
		% within Group	51.3%	23.3%	30.3%
Total		Count	39	116	155
		% within CRP Status	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

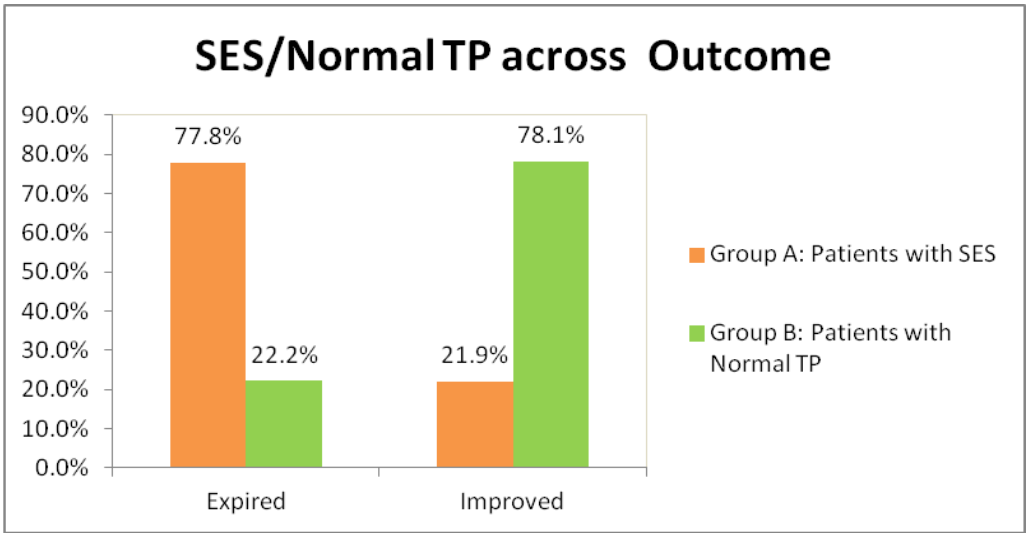
	Value	df	P-value
Pearson Chi-Square	10.835	1	.001
N of Valid Cases	155		

42.6% of CRP positive ACS patients had SES but only 17.6% of CRP negative individuals had SES. This was proved statistically as significant.

9) According to outcome:

Outcome * Group Crosstabulation

			Group		
			Group A: Patients with SES	Group B: Patients with normal TP	Total
Outcome	Expired	Count	7	2	9
		% within Outcome	77.8%	22.2%	100.0%
		% within Group	17.9%	1.7%	5.8%
	Improved	Count	32	114	146
		% within Outcome	21.9%	78.1%	100.0%
		% within Group	82.1%	98.3%	94.2%
Total		Count	39	116	155
		% within Outcome	25.2%	74.8%	100.0%
		% within Group	100.0%	100.0%	100.0%



Chi-Square Tests

	Value	df	P-value
Pearson Chi-Square	14.048	1	.002
N of Valid Cases	155		

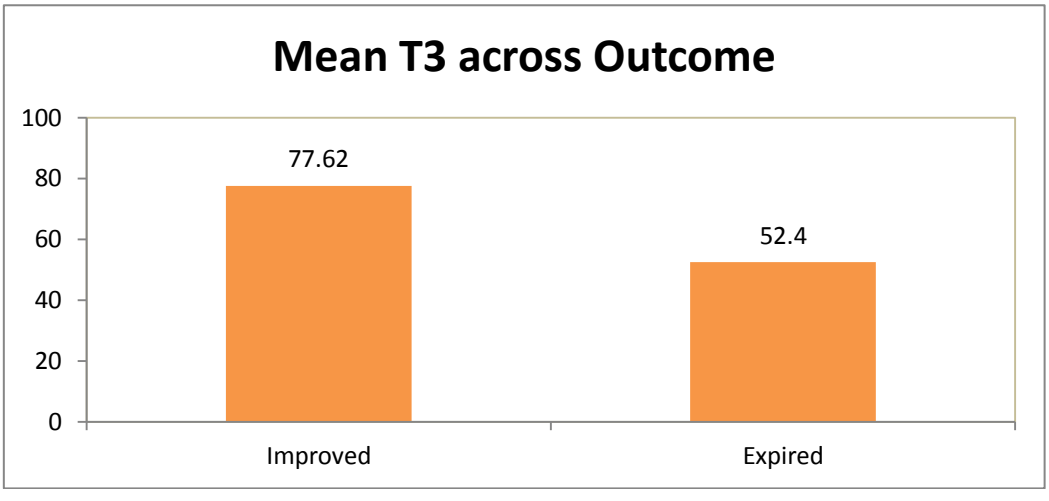
Nine out of 155 patients died. 21.9% of improved patients had SES where as 77.8% of patients who expired had SES. This was statistically significant. Hence it is concluded that SES was associated with worst outcome.

III) Study of correlation between the thyroid profile and the outcome among the SES patients with Acute Coronary Syndrome:

1) Correlation between T3 value and outcome:

Group Statistics

	Outcome	N	Mean	Std. Deviation	Std. Error Mean
T3	Improved	146	77.6233	13.18313	1.09104
	Expired	9	52.4444	17.37895	5.79298



Independent Samples Test

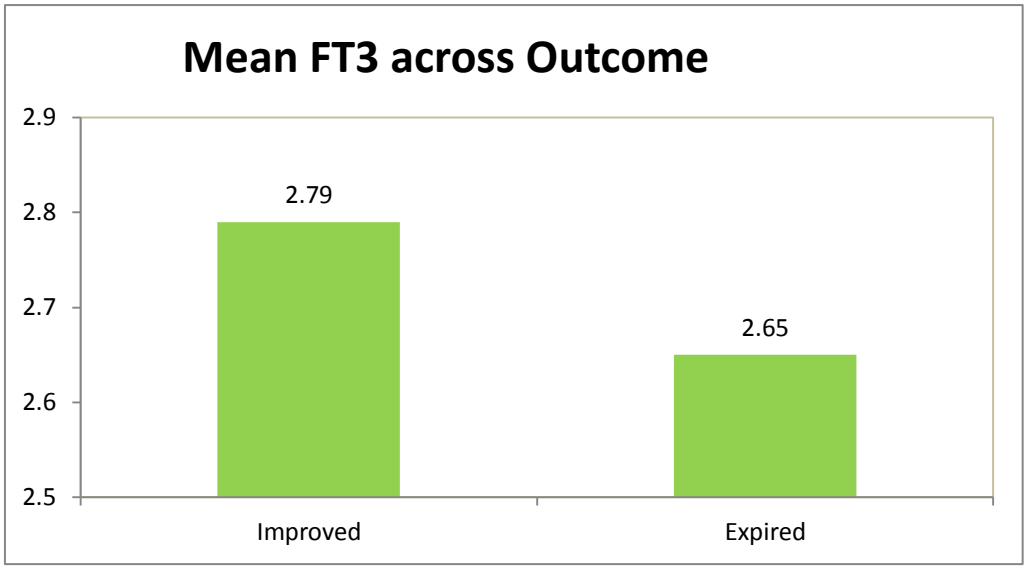
	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	P-value	Mean Difference	Std. Error Difference	Lower	Upper
T3	5.457	153	.000	25.1788	4.61431	16.06286	34.29483

The mean Total T3 value for the patient who were improved during hospital stay was 77.62 (normal limit 70- 100 microgram/dl); where as the expired patients had very low mean i.e. 52.4. This was a statistically significant correlation.

2) Correlation between FT3 value and outcome:

Group Statistics

	Outcome	N	Mean	Std. Deviation	Std. Error Mean
FT3	Improved	146	2.7917	.56384	.04666
	Expired	9	2.6556	.70211	.23404



Independent Samples Test

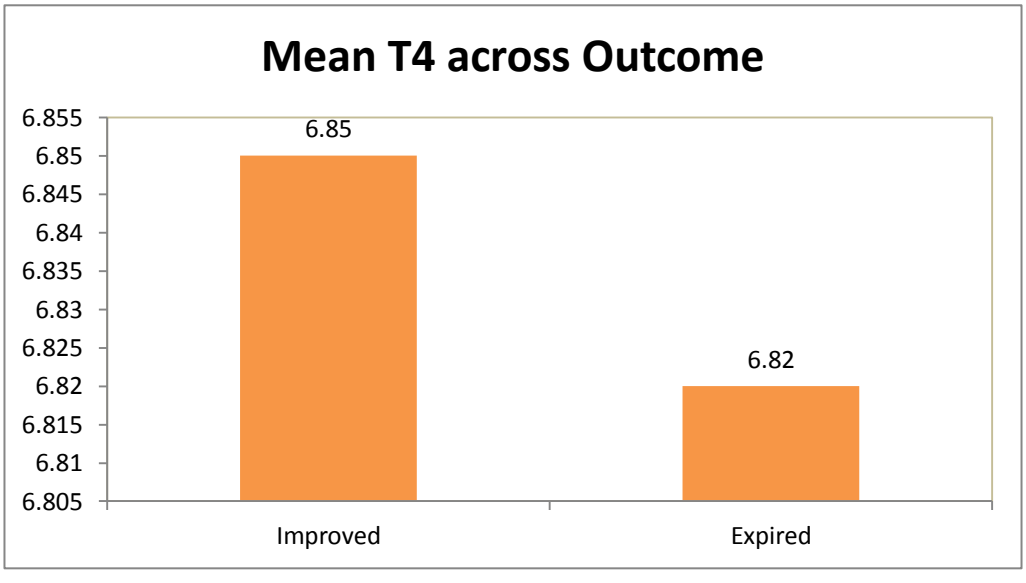
	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	P-value	Mean Difference	Std. Error Difference	Lower	Upper
FT3	.693	153	.489	.1362	.19642	-.25189	.52421

2.79 pg/ml was the mean value for the patients who were improved ; the expired patients had 2.65 pg/ml , but the difference was statistically not significant.

3) Correlation between T4 value and outcome:

Group Statistics

	Outcome	N	Mean	Std. Deviation	Std. Error Mean
t4	Improved	146	6.8506	1.97725	.16364
	Expired	9	6.8278	1.70747	.56916



Independent Samples Test

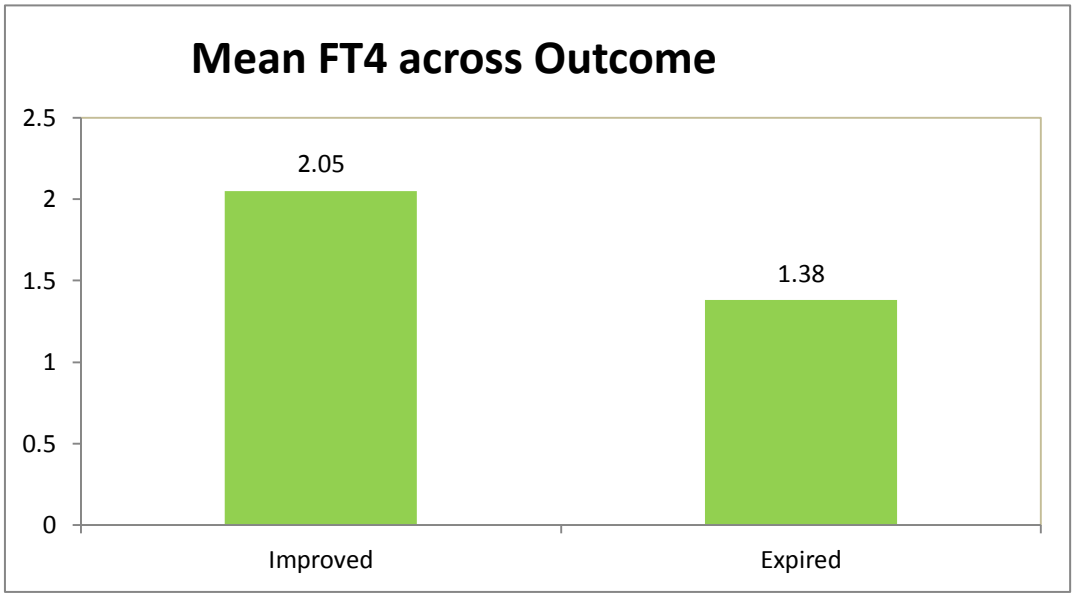
	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	P-value	Mean Difference	Std. Error Difference	Lower	Upper
t4	.034	153	.973	.0228	.67457	-1.30983	1.35550

Even though there was a difference in the mean values 6.85 & 6.82 µg/dl for the patients who were improved or progressed to death respectively, this difference was not significant by statistical analysis.

4) Correlation between FT4 value and outcome:

Group Statistics

	Outcome	N	Mean	Std. Deviation	Std. Error Mean
FT4	Improved	146	2.0525	7.50040	.62074
	Expired	9	1.3844	.21743	.07248



Independent Samples Test

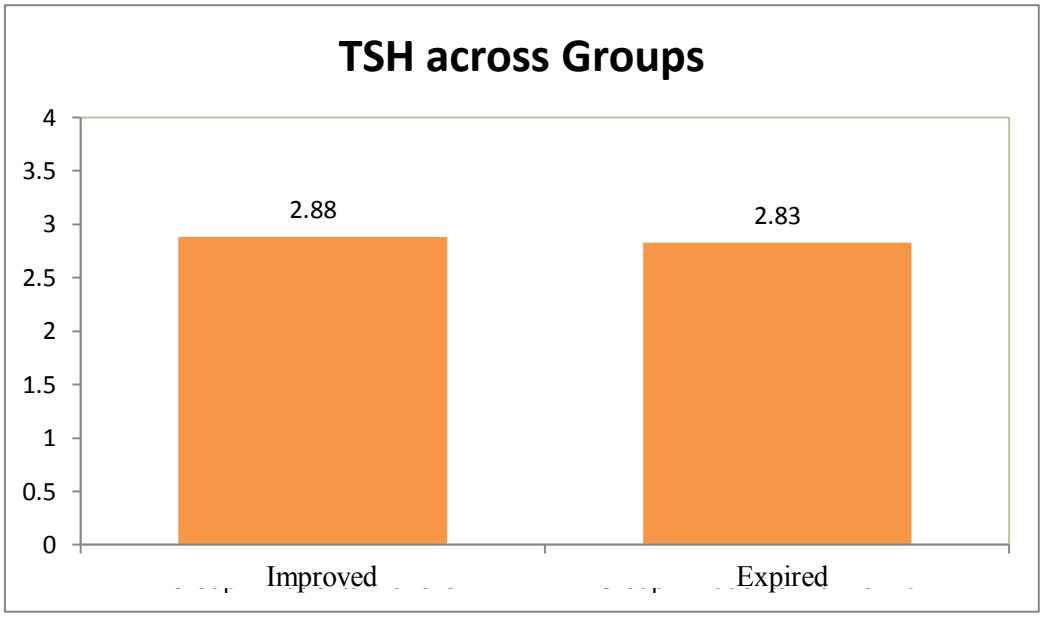
	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	P-value	Mean Difference	Std. Error Difference	Lower	Upper
FT4	.266	153	.790	.6680	2.50785	-4.28646	5.62250

1

2.05 ng/dl was the mean FT4 of improved patients and for the expired patients it was 1.38 ng/dl ; the difference was not significant.

5) Correlation between TSH value and outcome:

Group	N	Mean	Std. Deviation	Std. Error Mean
Group A Patient Improved	146	2.8833	.60750	.09728
Group B patient Expired	9	2.8371	.58773	.05457



Independent Samples Test

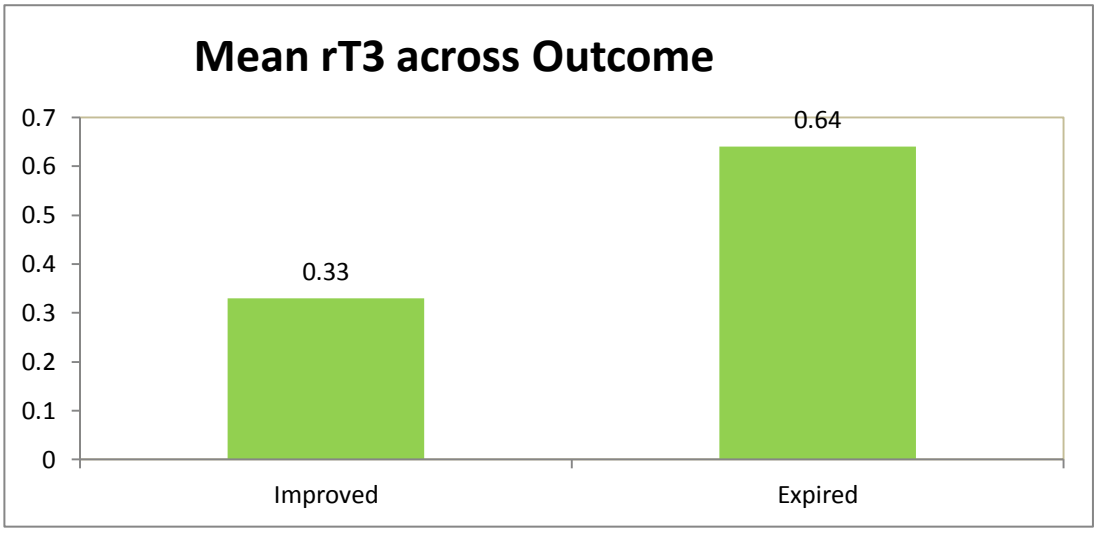
	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	P-value	Mean Difference	Std. Error Difference	Lower	Upper
TSH	.422	153	.674	.0463	.10971	-.17048	.26300

2.88 µIU/ml was the mean TSH of improved patients and for the expired paitents it was 2.83 µIU/ml. The difference was not significant statistically.

6) Correlation between rT3 value and outcome:

Group Statistics

	Outcome	N	Mean	Std. Deviation	Std. Error Mean
rT3	Improved	146	.3317	.13719	.01135
	Expired	9	.6433	.14440	.04813



Independent Samples Test

	t-test for Equality of Means						
						95% Confidence Interval of the Difference	
	t	df	P-value	Mean Difference	Std. Error Difference	Lower	Upper
rT3	-6.595	153	.000	-.3116	.04725	-.40497	-.21827

The mean rT3 value for the patients who were progressed to death or improved were 0.64 and 0.33 respectively. There was an association between and the high rT3 values and worst outcome.

DISCUSSION:

Acute Coronary Syndrome is one of the leading cause of mortality and morbidity both in India and in the worldwide.[2] The thyroid hormonal changes could result in the functional derangement of the cellular metabolism and affecting almost all the organs including the heart. This study was carried out with the aim of assessing the prevalence of one of the thyroidal hormonal derangement happening during any acute illness, the Sick Euthyroid Syndrome in patients with Acute Coronary Syndrome[9]. This study also assessed the distribution of SES in ACS and the correlation between thyroid hormone profiles with the outcome.

This study titled ***"Thyroid Profile in Acute coronary syndrome"*** was carried out in the Department of Medicine and in the Department of cardiology, kilpauk medical college and hospital (Chennai).

It is a Cross sectional study and was conducted during the period of November 2010 to October 2011(12 months).

I) The prevalence of Sick Euthyroid State in Acute Coronary Sndrome:

In this study of 155 Acute coronary Syndrome patients, 39 patients i.e. 25.2% (39/155) had Sick Euthyroid State. Remaining 74.8% (116/155) of ACS patients had normal thyroid profile. So the total unadjusted prevalence of SES in ACS patients is 25.2% .

This observation is similar to Ramsden DB[53], et al who reported the prevalence of SES in acute infarction was 22.7%

The prevalence of SES in different type of ACS as follows:

21.6% (8/37) of patients with Unstable angina had SES; 25.8% (8/31) of patients with STEMI IWMI had SES; 34.3% (12/35) of patients with STEMI ASMI had SES; 33.3% (3/9) of patients with Ext. AWMI had SES; 18.6% (8/43) of patients with NSTEMI had SES.

When we compared with the non SES group this prevalence rate not significant. Hence, the prevalence of SES in different type of ACS is same.

This observation is similar to *Rodrigo Caetano Pimentel et al.*[54] who reported that equal prevalence of SES in various types of ACS *But* Franklin JA et al reported that the incidence of SES was common after a myocardial infarction than Unstable Angina. This may be because of case selection in that study; He selected cases without matching the known confounding factors like systemic inflammatory conditions.

(III) Distribution of Sick Euthyroid Syndrome in ACS patients and Comparison study between Group A (ACS patients with SES) & Group B (ACS patients without SES) :

Age distribution of SES:

In this study, 33.3% (6/18) of SES patients were less than 40 years of age; 28.6% (26/91) of SES patients were in between 41 and 60 years of age; 15.2% (7/46) of SES patients were more than 60 years of age. The prevalence

of SES were equal in the first two groups but in case of older age group it was lesser. So, older age individuals are less vulnerable to develop SES. Even though there was significant difference in prevalence of SES between old age and younger age, the other confounding factors such as BMI to be considered. Because in our study, the mean BMI of old age patients was very less compared to younger age group. But the BMI was the strong predictor of SES in our study. This partially explained the low prevalence of SES in old age.

Wiersinga WA et al. reported in his study that the equal distribution of SES cases in all age group. But in our study we could not match the known confounding factors because of small number of cases. This explained why the old age people had lower incidence of SES.[58]

According to sex:

26.8% of females had SES and 24.5% of male patients had SES. P value was > 0.05 i.e. insignificant, the inference is that the occurrence of SES not influenced by sex.

Luiz Maurino et al. from Brazil reported that the incidence of SES after myocardial infarction was similar in both males and females. This is very similar to our study.[61]

According to BMI:

In the present study, 57.1% of SES patients were obese { BMI of >27.5} 21.4% of SES patients were overweight { BMI of 23.0 – 27.4 } 16.7% of SES patients had normal { BMI 18.5- 22.9}.

This also showed that 50% of people had BMI of < 18.5; but this should not be considered because only 2 patients were underweight . So, this will affect the over all statistical significance.

The statistical analysis showed the P value of 0.002 i.e., a significant association between the prevalence of SES and High BMI i.e. > 27.5 kg/m2.

There are several studies to support our observation in this study. Examples include Kliridis PA et al. reported the statistically significant effect of BMI in the incidence of SES after acute ischemic syndrome.[73]

According to Diabetic state:

29.5% of diabetics had SES; 18.3% of non diabetics had SES. The P value was 0.120 [69]; hence the association between diabetic state and prevalence of SES was statistically not significant.

This is similar to the observation of Langster W, et al from Philadelphia. He reported that statistically insignificant effect of diabetics in the incidence of SES after a MI[65].

According to Hypertension:

25.5% of Hypertensive patients had SES and 25.0% of normotensive patients had SES. Both the hypertensive patients and normotensives had the equal prevalence of SES. This was proved by statistical analysis.

Burman KD et al. reported the similar observation.[78]

According to Dyslipidemia:

31.1% of patients with dyslipidemia had SES when compared to 19.8% in case of patients with normal lipid profile. This association was statistically not significant.

This is similar to the report of Kanda T, et al. who stated in his study that statistically insignificant effect of dyslipidemia in the occurrence of SES in MI.[59]

According to smoking habit:

30.4% of smokers had SES when compared to 20.9% in non smokers.

P value was >0.01, hence the smoking habit did not influence the prevalence of SES.

Kotajima N, et al., reported that smoking did not affect the incidence of SES in ACS after matching the known confounding factors. This is similar to our study[67].

According to CRP:

42.6% of CRP positive ACS patients had SES but only 17.6% of CRP negative individuals had SES. There was a strong association between CRP status and the prevalence of SES. This was proved statistically as significant. P value 0.001.

Larsen PR et al. reported that incidence of SES after MI was 4 times greater in CRP positive group when compared to CRP negative group. In our study we reported that three times the risk of developing SES after MI[71].

According to outcome:

In this study nine out of one hundred and fifty five patients died. Out of the nine, seven patients had SES when compared with two patients in the normal thyroid profile group. The P value was 0.002 , significant; Hence it is concluded that SES was associated with worst outcome.

Escosteguy et al , one of the editors of The American Clinical Cardiology, reported in his study that the SES group of patients had worst outcome when compared to patients with normal thyroid profile[73].

III) Study of correlation between the thyroid profile and the outcome among the SES patients with Acute Coronary Syndrome:

1) Correlation between T3 value and outcome:

The mean Total T3 value for the patient who were improved during hospital stay was 77.62 (normal limit 70- 100 microgram/dl); where as the expired patients had very low mean i.e. 52.4. This was a statistically significant correlation. hence low total T3 level associated with worst outcome.

Michele Coceani, MD et al reported in his article named 'Thyroid Hormone and Coronary Artery Disease: From Clinical Correlations to Prognostic Implications' that low T 3 level positively correlated with the prognosis both for short term and long term. Barison A, et al. also reported the similar correlation. This is similar to our study observation.[70]

2. Correlation between FT3 value and outcome:

2.79 pg/ml was the mean value for the patients who were improved ; the expired patients had 2.65 pg/ml , but the difference was statistically not significant. So, FT3 value neither changed nor affecting the prognosis in SES.

Wartofsky et al reported the similar observation.

3. Correlation between T4 value and outcome:

Even though there was a difference in the mean values 6.85 & 6.82 ng/dl for the patients who were improved or progressed to death respectively, this difference was not significant by statistical analysis. T4 value was not changed in our study.

Kotajima N, et al reported T4 value may get reduced in severe cases[78]

4. Correlation between FT4 value and outcome:

2.05 ng/dl was the mean FT4 of improved patients and for the expired patients it was 1.38 n g/dl ; the difference was not significant. Hence the FT4 value will remain same in both worst out come group and better outcome group.

Yamada E, et al reported similar observation

5. Correlation between TSH value and outcome:

2.88 μIU/ml was the mean TSH of improved patients and for the expired paitents it was 2.83 μIU/ml. The difference was not significant statistically. Hence the TSH value will remain same in both worst out come group and better outcome group.[70]

Tauber JL. et al reported that in case of very sick condition T4 also reduced; but the TSH should be within normal limits[75]

6. Correlation between rT3 value and outcome:

The mean rT3 value for the patients who were progressed to death or improved were 0.64 and 0.33 respectively. There was an association between and the high rT3 values and worst outcome.

Utiger RD.et al reported that the rT3 is well correlated with high mortality [71]

This is similar to our observation.

SUMMARY:

This study aimed at estimating the prevalence of sick euthroid state in patients with ACS and also to find out its correlation with various risk factors for CAD. Finally to study the correlation of thyroid hormone profiles with outcome.

The study sample included 155 ACS patients admitted in ICCU and in the Medical wards. Each patient was assessed clinically and by laboratory investigations.

Primary observations regarding Sick Euthyroid State in patients with Acute Coronary Syndrome:

- In the present study, The above table shows 25.2% (39/155) of patients with Acute Coronary Syndrome had Sick Euthyroid State.
- Sick Euthyroid state occurs in all type of ACS with equal proportion , even though there were statistically insignificant variation.
- Sick Euthyroid state occurs in all age group and low prevalence of this condition noted in old age group.
- Sick Euthyroid state significantly associated with High BMI, CRP positivity and this condition associated with worst outcome.

- Sick Euthyroid state did not significantly correlated with sex, diabetic state, hypertension, dyslipidemia and smoking.
- The T3 value well correlated with outcome i.e. low T3 associated worst outcome among SES patients.
- The rT3 value also well correlated with outcome i.e. high rT3 associated worst outcome among SES patients.

CONCLUSION:

Prevalence of Sick Euthyroid State is very common in patients with Acute Coronary Syndrome. Almost one quarter of ACS patients had SES.

Prevalence of SES in old age group is low as compared to younger population.

Sick Euthyroid state significantly associated with High BMI, CRP positivity and this condition associated with worst outcome. So SES is a strong prognostic indicator in acute coronary syndrome.

Sick Euthyroid state did not significantly correlated with sex, diabetic state, hypertension, dyslipidemia and smoking.

□□□The T3 and rT3 levels well correlated with the outcome

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Study of Thyroid Profile in Acute Coronary Syndrome:

Pro forma:

Name of the Patient :

Age: DOA:

Sex: DOD:

Occupation:

Socioeconomic status:

Address:

CLINICAL PROFILE:

Presenting complaints:

H/O Past illness:

General Examination:

Pallor Cyanosis Clubbing Icterus JVP

Thyroid swelling Lymphadenopathy Pedal edema

Vitals:

Pulse

BP

RR

Systemic examination:

CVS

RS P/A

CNS

ECG:

DIGNOSIS:

Risk factors:

Killips class:

TIMI Score:

BIOCHEMICAL PROFILE:

Complete Blood Count;

TC DC Hb% ESR

Urine Examination;

Sugar Albumin Deposit

Blood sugar

RBS

FBS

PPBS

Blood Urea

Serum Creatinine

Serum Electrolytes

Na K

Fasting Lipid profile

T Chol.

TGL

CPK MB

Fasting Thyroid profile: At 3rd day of admission

Free T3

Free T4

rT3

TSH

T3

T4

IMAGING PROFILE:

Chest X ray

Echocardiography

Course during In Hospital stay:

NAME	AGE	SEX	BMI	DM	SHT	DYSLIPD	SMOKING	TYPE OF ACS	CRP	ECHOCARDIOGRAM	THYROID PROFILE							OUTCOME
			Kg/m2							RWMA EF% LV Fn	T3(µg/dl)	FT3(pg/ml)	rT3(µg/dl)	T4(µg/dl)	FT4(µg/dl)	TSH(mU/ml)	INFERENCE	
Rajan	55	M	24.34	Yes	Yes	No	Yes	STEMI - AS	P	IVS , IV apex 35% Severe	47	2.87	0.57	9.64	1.43	3.57	SES	Improved
Krishnan	63	M	21.22	Yes	No	No	Yes	STEMI - IW	N	Lower IVS Inf wall 41% Mod	78	2.7	0.13	7.83	1.71	2.83	Normal	Improved
Kasiammal	67	F	19.84	No	Yes	Yes	No	STEMI- IW	N	Inf wall 49% Mild	97	3.11	0.21	11.68	1.27	1.63	N	Improved
Varatha rajan	60	M	26.8	No	Yes	Yes	Yes	NSTEMI	P	No RWMA 63% Normal	63	3.87	0.43	8.09	1.49	2.87	SES	Improved
Swaminathan	45	M	25.06	Yes	No	Yes	No	STEMI- AS	N	IV apex, ant wall 33% Severe	87	2.76	0.23	7.86	1.09	3.51	N	Improved
Zuleka bee	80	F	26.56	Yes	Yes	Yes	No	UA - CL III	N	No RWMA 67% Normal	79	3.67	0.19	8.93	0.98	3.70	N	Improved
Kesavan	62	M	27.68	Yes	Yes	Yes	No	STEMI- AS	P	IVS, Lat wall 47% Mod	57	1.89	0.63	5.65	0.97	2.37	SES	Improved
Mohana sundaram	53	M	26.56	Yes	Yes	No	No	NSTEMI	N	No 65% Normal	93	2.31	0.13	4.87	1.31	3.42	N	Improved
Kuttiammal	60	F	17.66	No	Yes	No	No	UA - CL III	N	No 68% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Selvaraj	52	M	22.34	No	Yes	No	Yes	UA - CL III	N	No 60% Normal	51	2.97	0.53	7.83	1.09	2.24	SES	Improved
Elango	52	M	24.45	Yes	No	Yes	Yes	STEMI- AS	N	IVS , IV apex 37% Severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Rajeswari	71	F	23.21	Yes	Yes	No	No	STEMI- IW	P	Lower IVS Inf wall 40% Mod	62	3.11	0.43	8.60	1.73	2.87	SES	Improved
Sakunthala	70	F	24.64	No	Yes	Yes	No	UA - CL III	N	No 63% Normal	93	2.61	0.25	5.31	1.59	3.87	N	Improved
Egavalli	58	F	26.46	Yes	Yes	No	No	NSTEMI	N	LV apex 54% mild	88	2.21	0.37	5.30	1.02	2.97	N	Improved
Sekar	37	M	28.66	Yes	No	Yes	Yes	STEMI- Ext.AW	N	Ant&Lat wall 25% severe	73	2.69	0.20	5.36	1.12	3.87	N	Improved
Nirmal narendar	35	M	27.55	Yes	Yes	Yes	Yes	STEMI- Ext.AW	P	Global 25% severe	33	2.12	0.78	4.60	1.56	0.76	SES	**Expired**
Muniammal	70	F	22.86	Yes	No	No	No	UA - CL III	N	No 68% Normal	73	3.81	0.37	4.99	1.56	2.77	N	Improved
Rajendran	39	M	25.78	No	Yes	Yes	Yes	NSTEMI	N	No 63% Normal	89	2.90	0.17	7.30	1.02	1.87	N	Improved
Kannappan	36	M	24.68	No	Yes	Yes	Yes	STEMI- AS	N	IVS , IV apex 30% Severe	93	2.61	0.21	7.39	0.92	2.87	N	Improved
Dass	45	M	25.64	Yes	Yes	No	Yes	NSTEMI	P	LV apex 55% Adequate	83	3.67	0.30	6.09	1.52	2.50	N	Improved
Gopalakishnan	60	M	26.66	Yes	No	No	Yes	UA - CL III	N	No 63% Normal	72	3.78	0.37	5.39	1.92	3.87	N	Improved
Thirugnana sundari	56	F	24.65	No	Yes	Yes	No	NSTEMI	N	No 63% Normal	80	3.03	0.26	6.47	1.06	2.87	Normal	Improved
Balaji	43	M	27.88	Yes	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex 37% Severe	41	3.38	0.79	7.35	1.25	2.39	SES	**Expired**
Iqbal	46	M	28.82	Yes	Yes	Yes	No	STEMI- IW	P	Lower IVS Inf wall 48% Mod	57	1.89	0.51	6.72	0.97	3.85	SES	Improved
Ramu	43	M	26.44	Yes	No	No	Yes	NSTEMI	N	LV apex 54% mild	79	3.67	0.09	10.33	2.57	0.77	N	Improved
Rathika	63	F	19.9	No	Yes	No	No	UA - CL III	N	No 63% Normal	69	4.01	0.37	8.39	1.50	3.89	N	Improved
Panchammal	59	F	24.42	Yes	Yes	No	No	STEMI- IW	P	Lower IVS Inf wall 48% Mod	83	2.61	0.25	5.39	1.72	2.27	N	Improved
Kandasamy	55	M	20.04	No	Yes	No	No	NSTEMI	N	No 63% Normal	87	3.51	0.30	8.79	092	2.87	N	Improved
Jameela	75	F	26.68	Yes	Yes	Yes	No	STEMI- IW	N	Lower IVS Inf wall 48% Mod	80	2.89	0.27	5.35	1.07	2.86	N	Improved

Luisraj	50	M	23.42	Yes	No	No	No	UA - CL III	N	No	63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Jaya	69	F	19.84	Yes	Yes	No	No	UA - CL III	N	No	63% Normal	54	3.33	0.47	4.49	1.02	2.56	SES	Improved
Govindaraj	47	M	25.66	Yes	Yes	No	Yes	STEMI- AS	N	IVS , IV apex	37% Severe	83	3.61	0.23	6.39	1.42	3.07	N	Improved
Subha rao	30	M	28.48	Yes	Yes	Yes	Yes	STEMI- Ext.AW	P	Global	25% severe	51	2.76	0.68	4.98	1.22	0.49	SES	**Expired**
Durai raj	63	M	24.44	Yes	No	No	Yes	UA - CL III	N	No	70% Normal	90	2.61	0.31	5.81	1.70	2.07	N	Improved
Sowbakiyam	65	M	20.88	No	Yes	No	No	NSTEMI	N	No	60% Normal	93	2.60	0.17	5.39	1.52	2.87	N	Improved
Kuppan	55	M	22.38	No	Yes	Yes	No	NSTEMI	N	No	63% Normal	79	3.31	0.31	5.84	1.28	3.48	N	Improved
Kubendran	52	M	24.22	No	Yes	Yes	Yes	STEMI- IW	P	Lower IVS Inf wall	48% Mild	91	1.89	0.19	7.48	1.07	3.87	N	Improved
Shankari	45	F	25.06	Yes	No	No	Yes	STEMI- AS	P	IVS , IV apex	37% Mod	59	1.89	0.43	4.93	1.72	2.87	SES	Improved
kumari	60	F	26.68	Yes	Yes	Yes	No	STEMI- AS	N	IVS , IV apex	37% Mod	80	2.61	0.27	10.39	1.52	2.07	N	Improved
Abdul majeed	40	M	26.44	Yes	Yes	No	No	UA - CL III	N	No	65% Normal	76	2.71	0.48	7.69	1.52	2.09	N	Improved
Stalin	42	M	23.48	No	Yes	Yes	Yes	NSTEMI	P	No	63% Normal	83	2.73	0.27	7.30	1.52	2.07	N	Improved
Muniyappan	43	M	26.14	No	Yes	Yes	Yes	NSTEMI	N	LV apex	54% adequate	60	2.65	0.49	7.53	1.03	3.38	SES	Improved
Subhuraj	60	M	24.9	Yes	No	No	Yes	STEMI- AS	N	IVS , IV apex	39% Mod	83	2.61	0.37	5.39	1.50	2.82	N	**Expired**
Ponnammal	52	F	19.98	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall	48% Mild	53	3.05	0.51	6.98	1.28	1.04	SES	Improved
Sivakumar	40	M	24.04	No	Yes	No	Yes	UA - CL III	N	No	70% Normal	99	3.61	0.27	5.39	1.52	2.87	N	Improved
Kandasamy	52	M	22.56	No	Yes	No	Yes	NSTEMI	P	No	63% Normal	73	2.91	0.20	7.39	0.92	2.09	N	Improved
Usha	47	F	27.84	Yes	Yes	Yes	No	STEMI- AS	N	IVS , IV apex	37% Mod	49	3.73	0.61	7.51	1.73	0.57	SES	**Expired**
Krishnan	65	M	23.9	No	Yes	No	No	UA - CL III	N	No	63% Normal	83	2.82	0.27	9.39	1.52	2.87	N	Improved
Soundaram	65	F	24.48	Yes	Yes	Yes	No	STEMI- IW	N	Lower IVS Inf wall	48% Mild	93	2.61	0.27	5.39	1.59	2.87	N	Improved
Rajammal	74	F	19.24	No	Yes	No	No	UA - CL III	N	No	67% Normal	83	3.67	0.29	5.07	1.91	2.38	N	Improved
Palani	40	M	27.88	Yes	Yes	No	Yes	STEMI- AS	P	IVS , IV apex	30% Severe	83	1.89	0.35	11.89	1.27	3.28	N	Improved
Gnanasekar	48	M	26.68	Yes	No	Yes	Yes	STEMI- IW	N	Lower IVS Inf wall	48% Mild	61	3.71	0.43	8.04	1.41	0.93	SES	Improved
Padmavathy	57	F	20.08	No	Yes	No	No	NSTEMI	N	LV apex	54% adeq	83	2.61	0.27	5.39	1.52	2.07	N	Improved
Sakthivel	24	M	28.42	Yes	Yes	Yes	Yes	STEMI- Ext.AW	P	Global	25% severe	80	2.61	0.31	8.24	1.70	2.87	N	Improved
Selvakumar	39	M	24.78	Yes	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex	37% Mod	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Rajathi	45	F	23.64	Yes	No	No	No	UA - CL III	N	No	62% Normal	54	1.68	0.49	7.83	0.85	4.02	SES	Improved
Rangasamy	55	M	22.86	No	No	Yes	No	NSTEMI	N	No	63% Normal	66	2.41	0.49	4.90	1.09	2.89	SES	Improved
Sakunthala	67	F	24.82	Yes	No	Yes	No	STEMI- IW	N	Lower IVS	50% adequate	91	1.89	0.30	8.21	1.34	3.28	N	Improved
Ganapathy	35	M	25.06	No	Yes	Yes	Yes	STEMI- IW	N	Lower IVS Inf wall	48% Mild	98	2.61	0.34	5.39	1.07	2.80	N	Improved
Harikrishnan	54	M	23.82	No	No	Yes	Yes	NSTEMI	N	LV apex	54% adequate	83	2.67	0.27	7.82	1.52	2.87	N	Improved
Punitha	58	F	24.64	Yes	No	No	No	UA - CL III	N	No	63% Normal	72	4.0	0.32	5.39	0.97	3.78	N	Improved
Devendran	47	M	25.68	Yes	Yes	No	Yes	STEMI- IW	P	Lower IVS Inf wall	48% Mild	83	2.61	0.27	5.39	1.24	1.89	N	Improved
Natarajan	60	M	23.64	No	Yes	No	No	NSTEMI	N	LV apex	54% Adequate	57	3.57	0.60	11.03	1.78	0.43	SES	Improved
Selvaraj	49	M	26.82	Yes	No	Yes	Yes	STEMI- AS	N	IVS , IV apex	37% Mod	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Abdullah	49	M	25.66	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall	48% Mild	69	3.84	0.30	11.25	1.70	3.99	N	Improved

Abdullah	49	M	25.66	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall 48% Mild	69	3.84	0.30	11.25	1.70	3.99	N	Improved
Arumugam	30	M	27.84	Yes	No	Yes	Yes	STEMI- AS	P	IVS , IV apex 37% Mod	59	3.42	0.63	6.72	1.27	0.57	SES	Improved
Nazeemunnisa	60	F	26.86	Yes	No	Yes	No	NSTEMI	N	No 65% Normal	93	2.48	0.27	5.39	1.50	2.89	N	Improved
Velankanni	45	F	24.48	Yes	Yes	No	No	UA - CL III	N	No 63% Normal	79	1.99	0.31	10.84	1.09	2.87	N	Improved
Kuppan	39	M	24.82	No	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex 47% Mild	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Sivasankari	44	F	23.44	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall 48% Mild	37	2.87	0.79	10.15	1.01	0.92	SES	**Expired**
Kesavan	45	M	26.22	Yes	Yes	No	Yes	STEMI- AS	N	IVS , IV apex 38% Mod	83	2.61	0.27	5.39	1.52	4.09	N	Improved
Suseela	55	F	19.9	No	Yes	Yes	No	UA - CL III	N	No 60% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Jayachandran	50	M	21.24	No	Yes	No	Yes	UA - CL III	N	No 67% Normal	49	3.51	0.63	7.21	1.82	0.57	SES	Improved
Sampantham	58	M	24.84	Yes	No	No	No	NSTEMI	N	No 63% Normal	83	1.95	0.27	6.89	0.96	2.87	N	Improved
Jothi	48	F	27.57	Yes	Yes	Yes	No	STEMI- AS	N	IVS , IV apex 39% Mod	103	2.61	0.27	5.39	1.52	3.02	N	Improved
Indrani	60	F	20.08	No	Yes	No	No	NSTEMI	N	No 63% Normal	53	2.09	0.58	7.29	1.26	3.04	SES	Improved
Radha	49	F	23.57	Yes	Yes	No	No	NSTEMI	N	No 64% Normal	91	2.61	0.27	5.39	1.52	2.87	N	Improved
Hendry	49	M	23.53	No	No	Yes	Yes	UA - CL III	P	No 69% Normal	83	2.40	0.32	5.39	1.78	3.05	N	Improved
Balu	44	M	27.37	Yes	Yes	Yes	Yes	STEMI- AS	N	IVS , IV apex 42% Mod	94	2.61	0.27	10.90	1.52	3.41	N	Improved
Sekar	47	M	25.95	Yes	No	Yes	Yes	STEMI- Ext.AW	P	Global 25% severe	57	1.34	0.67	5.43	1.72	2.30	SES	Improved
Venkatesan	45	M	26.44	Yes	Yes	No	Yes	STEMI- AS	N	Ant wall, IV apex 35% Severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Chandrasekar	46	M	22.87	No	Yes	No	Yes	NSTEMI	N	No 63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Ganesamoorthy	40	M	28.45	Yes	No	Yes	Yes	STEMI- AS	P	IVS , IV apex 39% Mod	49	2.43	0.57	6.47	1.37	1.89	SES	Improved
Nirmala	44	F	21.09	No	Yes	No	No	UA - CL III	N	No 60% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Elumalai	55	M	22.66	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall 38% Mod	92	2.61	0.34	11.09	1.76	3.21	N	Improved
Saroja	70	F	21.83	No	Yes	No	No	UA - CL III	N	No 60% Normal	59	2.65	0.61	5.30	1.00	2.31	SES	Improved
Mohammada bee	58	F	24.48	Yes	No	Yes	No	NSTEMI	N	No 63% Normal	78	3.61	0.32	8.39	1.57	2.07	N	Improved
Padmanaban	67	M	26.33	Yes	No	Yes	No	NSTEMI	N	No 68% Normal	90	2.61	0.37	12.04	1.70	3.41	N	Improved
Samikannu	60	M	22.64	No	No	Yes	No	STEMI- IW	P	Lower IVS Inf wall 48% Mild	86	2.69	0.20	8.97	1.52	2.83	N	Improved
Venkatesan	31	M	28.54	Yes	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex 39% Mod	42	1.76	0.72	5.31	0.92	0.97	SES	Improved
Govindammal	75	F	19.42	No	Yes	No	No	UA - CL III	N	No 65% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Muniammal	60	F	22.65	Yes	Yes	No	No	NSTEMI	N	No 63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Shanmugam	49	M	26.55	Yes	Yes	Yes	Yes	STEMI- Ext.AW	P	Ant, Lat wall 35% severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Mannu	49	M	22.89	No	Yes	No	Yes	NSTEMI	P	No 63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Govindasamy	65	M	21.87	No	Yes	Yes	No	STEMI- AS	N	IVS , IV apex 40% Mod	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Velu	38	M	27.65	Yes	Yes	Yes	Yes	STEMI- AS	N	IVS , IV apex 30% Severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Pavithra kumar	45	M	25.34	Yes	No	Yes	Yes	STEMI- IW	N	Lower IVS Inf wall 48% Mild	42	1.87	0.74	5.27	0.93	0.33	SES	Improved
Kannathal	65	F	21.56	yes	No	No	No	STEMI- IW	P	Inf wall 56% adeq	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Settu	45	M	24.33	No	Yes	No	Yes	NSTEMI	N	No 64% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved

Hendry	49	M	23.53	No	No	Yes	Yes	UA - CL III	P	No	69% Normal	83	2.40	0.32	5.39	1.78	3.05	N	Improved
Balu	44	M	27.37	Yes	Yes	Yes	Yes	STEMI- AS	N	IVS , IV apex	42% Mod	94	2.61	0.27	10.90	1.52	3.41	N	Improved
Sekar	47	M	25.95	Yes	No	Yes	Yes	STEMI- Ext.AW	P	Global	25% severe	57	1.34	0.67	5.43	1.72	2.30	SES	Improved
Venkatesan	45	M	26.44	Yes	Yes	No	Yes	STEMI- AS	N	Ant wall, IV apex	35% Severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Chandrasekar	46	M	22.87	No	Yes	No	Yes	NSTEMI	N	No	63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Ganesamoorthy	40	M	28.45	Yes	No	Yes	Yes	STEMI- AS	P	IVS , IV apex	39% Mod	49	2.43	0.57	6.47	1.37	1.89	SES	Improved
Nirmala	44	F	21.09	No	Yes	No	No	UA - CL III	N	No	60% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Elumalai	55	M	22.66	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall	38% Mod	92	2.61	0.34	11.09	1.76	3.21	N	Improved
Saroja	70	F	21.83	No	Yes	No	No	UA - CL III	N	No	60% Normal	59	2.65	0.61	5.30	1.00	2.31	SES	Improved
Mohammada bee	58	F	24.48	Yes	No	Yes	No	NSTEMI	N	No	63% Normal	78	3.61	0.32	8.39	1.57	2.07	N	Improved
Padmanaban	67	M	26.33	Yes	No	Yes	No	NSTEMI	N	No	68% Normal	90	2.61	0.37	12.04	1.70	3.41	N	Improved
Samikannu	60	M	22.64	No	No	Yes	No	STEMI- IW	P	Lower IVS Inf wall	48% Mild	86	2.69	0.20	8.97	1.52	2.83	N	Improved
Venkatesan	31	M	28.54	Yes	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex	39% Mod	42	1.76	0.72	5.31	0.92	0.97	SES	Improved
Govindammal	75	F	19.42	No	Yes	No	No	UA - CL III	N	No	65% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Muniammal	60	F	22.65	Yes	Yes	No	No	NSTEMI	N	No	63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Shanmugam	49	M	26.55	Yes	Yes	Yes	Yes	STEMI- Ext.AW	P	Ant, Lat wall	35% severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Mannu	49	M	22.89	No	Yes	No	Yes	NSTEMI	P	No	63% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Govindasamy	65	M	21.87	No	Yes	Yes	No	STEMI- AS	N	IVS , IV apex	40% Mod	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Velu	38	M	27.65	Yes	Yes	Yes	Yes	STEMI- AS	N	IVS , IV apex	30% Severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Pavithra kumar	45	M	25.34	Yes	No	Yes	Yes	STEMI- IW	N	Lower IVS Inf wall	48% Mild	42	1.87	0.74	5.27	0.93	0.33	SES	Improved
Kannathal	65	F	21.56	yes	No	No	No	STEMI- IW	P	Inf wall	56% adeq	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Settu	45	M	24.33	No	Yes	No	Yes	NSTEMI	N	No	64% Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Saravanan	32	M	28.89	Yes	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex	37% Mod	42	2.43	0.67	6.47	1.28	3.89	SES	**Expired**

Thirunavukkarasu	45	M	26.43	Yes	No	No	Yes	UA - CL III	N	No	63%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Dhandabani	45	M	28.54	Yes	Yes	Yes	Yes	STEMI- Ext.AW	N	Global	25%	severe	83	2.61	0.27	5.70	1.23	2.90	N	Improved
Suresh	53	M	22.43	No	Yes	No	No	NSTEMI	N	LV apex	54%	adequate	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Gayathri	51	F	21.34	No	Yes	No	No	UA - CL III	P	No	63%	Normal	89	2.61	0.27	10.87	1.50	2.87	N	Improved
Kumutha	67	F	22.45	No	No	Yes	No	UA - CL III	N	No	53%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Santhosam	57	M	24.76	Yes	Yes	No	Yes	NSTEMI	N	LV apex	54%	Adequate	60	3.81	0.43	9.73	1.27	3.92	SES	Improved
Rani	56	F	21.54	No	Yes	No	No	NSTEMI	N	No	63%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Joseph	63	M	26.54	Yes	No	Yes	Yes	STEMI- IW	P	Lower IVS Inf wall	48%	Mild	54	2.87	0.69	6.27	1.37	2.83	SES	Improved
Ramaiya	57	M	24.58	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall	47%	Mild	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Rajammal	78	F	19.08	No	Yes	No	No	UA - CL III	N	No	62%	Normal	80	2.61	0.37	5.39	1.75	2.87	N	Improved
Kumaran	67	M	25.83	Yes	No	No	Yes	NSTEMI	N	No	69%	Normal	83	3.86	0.35	10.98	1.70	3.40	N	Improved
Sarangapani	54	M	23.54	Yes	No	No	Yes	STEMI- IW	P	Lower IVS Inf wall	48%	Mild	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Kokilammal	65	F	21.58	No	Yes	Yes	No	NSTEMI	N	No	60%	Normal	78	2.76	0.07	7.39	1.82	2.07	N	Improved
Palaniyammal	69	F	19.98	No	Yes	Yes	No	UA - CL III	P	No	63%	Normal	61	3.67	0.49	8.63	1.09	3.30	SES	Improved
Rajasekar	49	M	25.61	Yes	No	No	Yes	STEMI- AS	N	IVS , IV apex	33%	Severe	87	2.11	0.36	12.65	1.70	3.87	N	Improved
Moorthy	52	M	26.83	Yes	Yes	Yes	No	NSTEMI	N	LV apex	54%	Adequate	87	2.43	0.29	8.39	1.57	2.80	N	Improved
Batcha	63	M	28.88	Yes	Yes	Yes	No	STEMI- IW	N	Lower IVS Inf wall	48%	Mild	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Rangarajan	49	M	26.63	Yes	Yes	Yes	No	STEMI- AS	P	IVS , IV apex	33%	Severe	83	2.60	0.35	5.98	1.32	3.87	N	Improved
Poongodi	54	F	24.48	Yes	No	Yes	No	UA - CL III	N	No	67%	Normal	59	3.87	0.50	7.43	1.41	2.59	SES	Improved
Kathiravan	46	M	24.45	No	Yes	No	Yes	NSTEMI	N	No	63%	Normal	80	3.24	0.35	10.67	1.52	2.86	N	Improved
Dharani	52	F	22.06	Yes	No	No	No	STEMI- IW	P	Lower IVS Inf wall	48%	Mod	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Subbaiah	67	M	23.78	No	Yes	No	Yes	UA - CL III	N	No	60%	Normal	98	2.67	0.09	5.30	1.09	2.98	N	Improved
Kaliammal	73	F	18.08	No	Yes	No	No	NSTEMI	N	LV apex	54%	mild	64	3.61	0.42	7.34	1.27	3.38	SES	Improved
Lakshmiammal	64	F	21.9	Yes	No	No	No	UA - CL III	N	No	69%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Babu	39	M	26.87	Yes	No	Yes	Yes	STEMI- Ext.AW	P	Global	25%	severe	80	2.91	0.30	11.39	1.07	2.08	N	Improved
Kamal basha	49	M	23.87	Yes	No	No	Yes	UA - CL III	N	No	63%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Murugan	57	M	21.76	No	Yes	Yes	No	NSTEMI	N	No	67%	Normal	97	3.85	0.37	7.39	1.54	2.07	N	Improved
Rajammal	68	F	22.43	Yes	No	No	No	STEMI- IW	N	Lower IVS Inf wall	45%	Mild	87	2.60	0.29	5.09	1.52	2.89	N	Improved
Murugeswari	49	F	26.89	Yes	Yes	Yes	No	STEMI- AS	P	IVS , IV apex	39%	Mod	49	3.85	0.79	6.34	1.63	0.97	SES	Improved
Muthammal	53	F	20.65	No	Yes	Yes	No	NSTEMI	N	No	70%	Normal	83	2.61	0.20	5.98	1.09	2.87	N	Improved
Kannan	43	M	26.45	No	Yes	No	Yes	NSTEMI	N	No	66%	Normal	57	2.95	0.49	7.82	1.59	0.72	SES	Improved
Senthil	59	M	22.43	No	Yes	Yes	Yes	UA - CL III	N	No	69%	Normal	83	2.01	0.27	5.39	1.52	3.98	N	Improved
Ramalingam	67	M	21.81	Yes	No	No	Yes	STEMI- IW	N	Lower IVS Inf wall	48%	Mod	89	2.61	0.35	9.39	1.93	2.87	N	Improved
Burhana	63	F	24.56	Yes	No	No	No	UA - CL III	N	No	60%	Normal	83	2.67	0.20	5.19	1.20	2.56	N	Improved
Kuselan	72	M	21.73	No	Yes	No	No	NSTEMI	N	LV apex	54%	mild	80	3.11	0.27	10.9	1.92	2.08	N	Improved
Raja kannan	47	M	27.89	Yes	No	Yes	Yes	STEMI- AS	P	IVS , IV apex	37%	Severe	80	2.71	0.45	5.98	1.52	2.80	N	Improved
Muthukumari	69	F	19.02	No	Yes	No	No	STEMI- IW	N	Lower IVS Inf wall	48%	Mod	83	2.61	0.27	5.39	1.52	2.87	N	Improved

Ganesan	73	M	23.31	No	Yes	Yes	No	NSTEMI	N	No	69%	Normal	78	2.01	0.30	5.33	1.12	2.91	N	Improved
Rukmaniammal	67	F	20.98	No	Yes	Yes	No	STEMI- IW	P	Lower IVS Inf wall	48%	Mod	83	2.74	0.20	8.39	1.92	2.28	N	Improved
Manikandan	50	M	26.43	Yes	No	Yes	Yes	STEMI- AS	P	IVS , IV apex	37%	Severe	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Suresh kumar	41	M	27.87	Yes	Yes	Yes	Yes	STEMI- Ext.AW	P	Ant, Lat wall	25%	severe	70	3.41	0.33	7.87	1.07	3.94	N	Improved
Ramani	47	M	28.43	Yes	Yes	Yes	Yes	STEMI- AS	P	IVS , IV apex	34%	Severe	49	3.19	0.63	7.82	1.63	1.25	SES	Improved
Marimuthu	71	M	22.56	No	Yes	No	No	NSTEMI	N	No	65%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Ponnuthai	68	F	20.52	No	Yes	No	No	UA - CL III	N	No	63%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Kumaresan	51	M	26.65	Yes	No	No	Yes	UA - CL III	P	No	73%	Normal	75	3.97	0.34	5.39	1.87	0.57	N	Improved
Amutha	57	F	23.09	Yes	No	No	No	STEMI- IW	P	Lower IVS Inf wall	48%	Mild	60	1.29	0.62	7.31	1.39	3.83	SES	**Expired**
Duraisamy	71	M	23.09	No	Yes	Yes	No	NSTEMI	N	No	63%	Normal	83	2.61	0.27	5.39	1.52	2.87	N	Improved
Kumaran	65	M	21.78	No	Yes	No	No	NSTEMI	N	No	68%	Normal	83	2.48	0.35	5.34	1.57	2.17	N	Improved
Parasuraman	70	M	22.71	No	Yes	Yes	No	STEMI- AS	P	IVS , IV apex	37%	Mod	78	3.61	0.17	9.39	1.57	2.39	N	Improved
Janakiraman	65	M	24.54	Yes	No	No	Yes	STEMI- AS	P	IVS , IV apex	33%	Severe	83	2.89	0.27	5.41	1.09	2.10	N	Improved
Saraswathy	67	F	23.56	Yes	Yes	No	No	STEMI- IW	N	Lower IVS Inf wall	41%	Mod	90	2.61	0.26	5.30	1.52	2.27	N	Improved
Karuppayi	56	F	25.92	Yes	Yes	Yes	Yes	STEMI- AS	N	IVS	47%	Mild	55	2.37	0.58	7.83	1.27	2.68	SES	Improved
Thamaraikannan	49	M	27.55	Yes	No	Yes	No	UA - CL III	P	No	63%	Normal	61	3.80	0.42	6.90	1.49	2.51	SES	Improved
Umavathy	51	F	23.21	Yes	Yes	No	No	STEMI- IW	N	Lower IVS Inf wall	48%	Mild	83	2.69	0.20	5.30	1.02	2.08	N	Improved
Eswaran	63	M	24.55	Yes	No	Yes	No	STEMI- AS	N	IVS , IV apex	37%	Severe	78	1.48	0.10	7.92	1.34	2.87	N	Improved